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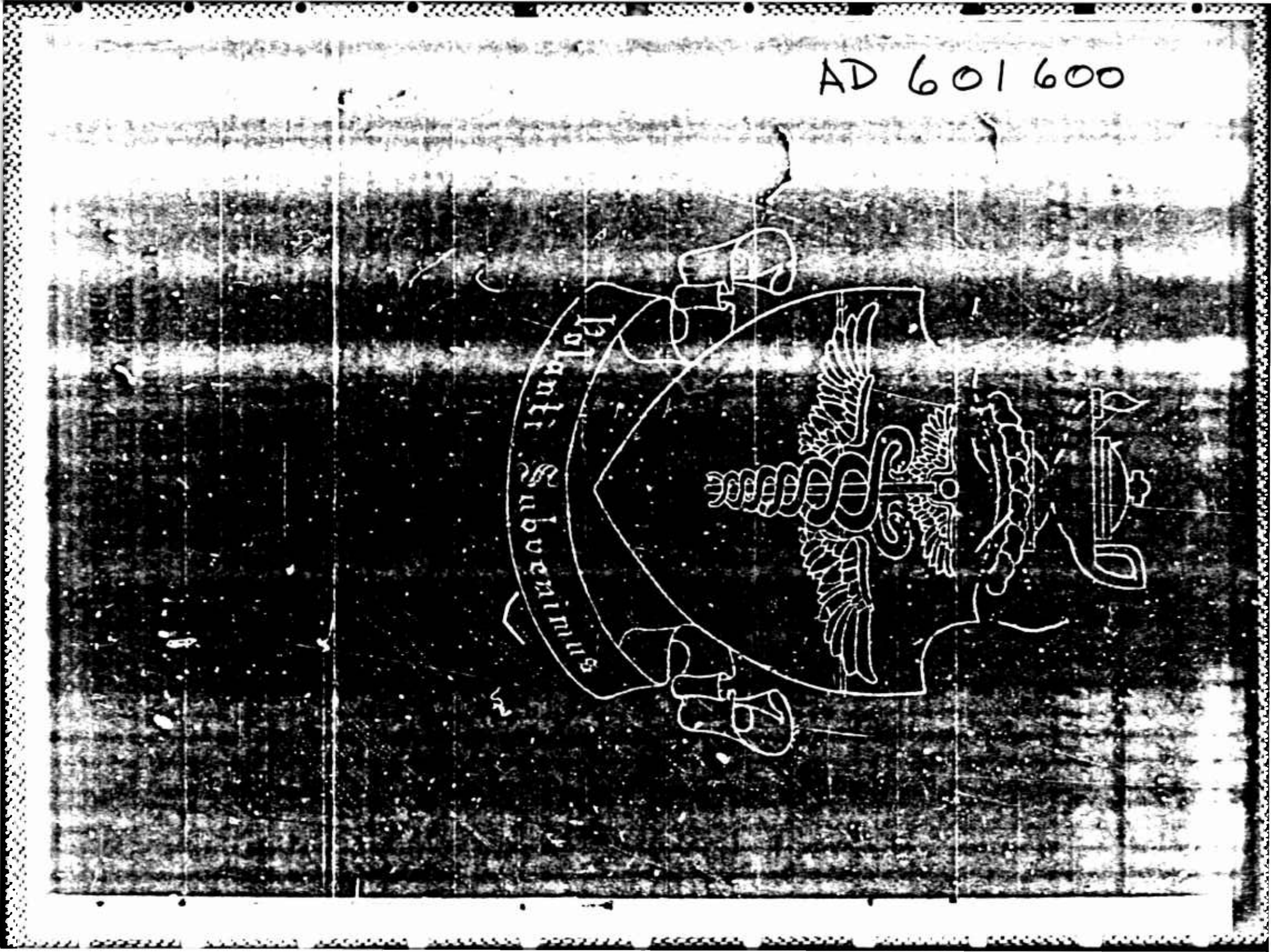

# DYSBARISM

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# FOREWORD

This manuscript was prepared in 1950 by Dr. Adler and has never been formally published. Notes have been passed from hand to hand, and references are given in many publications on decompression sickness to "Adler, H. F. *Dysbarism.* Unpublished Report." This report is regarded as a classic review by many investigators; it has withstood the test of time. To make this report available to all interested persons, it is being published in its original form.

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# DYSBARISM

## INTRODUCTION

This review is devoted to a detailed discussion of the various aspects of *dysbarism*, which is a new term replacing that of "decompression sickness." Many theoretic as well as experimental observations are presented, all of which are believed to be of interest and of importance. It cannot be overemphasized, however, that the greatest material benefits will be derived if constant efforts are made to keep clearly in mind the classification of dysbarism. Minor facts and details should not be allowed to obscure the more important general principles. It is definitely advantageous, for example, to make frequent reference to the principles of atmospheric physics—especially the factors related to the behavior of gases at altitude. It will be noted that the various aspects of aviation physiology are closely related and that an understanding of them is largely a matter of integrating newly presented material with what has gone before.

*Dysbarism is a term used to mean the symptoms and signs resulting from all changes in barometric pressure.* For the purpose of our discussion, however, most of the emphasis will be placed on changes in barometric pressure in which the total change in pressure is less than 760 mm. Hg as occurs in *altitude dysbarism. Caisson disease* consists of symptoms which result when humans have been exposed to high pressures and then are decompressed to lower pressures, the latter pressures being atmospheric or greater. Caisson disease will be considered only when such discussions are of general comparative interest or serve to aid in an understanding of the phenomena encountered in aviation medicine.

One should clearly keep in mind the concept that at sea level the barometric pressure is 760 mm. Hg and, no matter how high the aviator ascends before descent to sea level is made, the differential pressure between his peak altitude and that at sea level is some value less than 760 mm. Hg.

In comparison, the diver or workman in a diving bell, which is at a depth of several hundred feet below the surface of the sea, can be supplied with air or other gas mixture at a pressure of 4 or 5 atmospheres, which is equivalent to 3,040 and 3,800 mm. Hg. respectively. Obviously, on return to sea level, the total change in pressure to which his body has been exposed is greater than 760 mm. Hg. In either instance, however, the changes in pressure to which their bodies are exposed give rise to a number of clinical symptoms.

## HISTORICAL ASPECTS

Robert Boyle in 1670 exposed a viper to a very low ambient pressure and reported seeing a bubble within the eye. A French engineer, Triger, about 1850, built and used the first caisson for tunnel work. The first account of "compressed air illness" (caisson disease) was made by Pol and Watelle in 1854. Reference to the above papers and many other early workers are cited in the books by Paul Bert (131), Hill (129), and Armstrong (16). In their writing, Pol and Watelle noted numerous pathologic effects of caisson disease and presented data which showed that besides a number of less serious reactions several deaths occurred. Their remarkable conclusions were that compressions up to 4.5 atmospheres were not perilous, but that the subsequent decompression was the dangerous period. The danger was proportional to the degree and period of compression and especially the rapidity of decompression. They also indicated that decompression should be slow, and if symptoms occurred then recompression was the treatment and was to be followed by even slower decompression. In 1869 De Mericourt reported symptoms in sponge divers which were similar to those found in caisson workers. During the last half of the 19th century, many engineering projects in Europe

and America employed caissons resulting in a high morbidity and mortality from caisson disease. In 1878 Paul Bert published "La Pression Barométrique" (131) in which he indicated that the cause of the symptoms of caisson disease was the liberation of nitrogen gas bubbles. Among other facts, he demonstrated that if animals were put in an oxygen-rich atmosphere for some time before being rapidly decompressed, then no bubbles were formed. Heller et al., quoted by Hill (129), studied many cases of caisson disease, described the complex symptoms, and among other things, attributed the skin formication and painful itch to air bubbles produced in the fat of subcutaneous tissue. Keays in 1909 published a book in New York titled *Compressed Air Illness* and summarized 3,692 cases of caisson disease occurring in 10,000 men. There were 20 deaths. Hill's book (129) reviews much of the above literature and presents his own observations.

In 1929 Jongbloed presented a thesis to the University of Utrecht in Holland. He reported the effects of simulated ascent to high altitudes in a low pressure chamber. The content of this thesis was presented at the International Air Congress in 1930 (150). Protocols are given for tests at 6,000, 9,000, 12,000, and 14,000 meters with analysis of alveolar air at altitude. The report gave descriptions of bends in the wrists, knees, and hip joints, and attention was called to some of the similarities and differences between caisson disease and altitude dysbarism. Barcroft et al., quoted by Fulton (82), noted "sore legs" at 30,000 feet in a low pressure chamber and acute pain in both knees at 36,000 feet. These symptoms of bends were experienced in experiments conducted in 1931.

In this country, Armstrong (16) performed a number of experiments which were important to the development of aviation medicine and were included in the first edition of his book. Among these investigations was an account of bends at altitude experienced in a decompression chamber at Wright Field in 1934 (13). These studies, as well as a number to be considered later by Behnke of the U. S. Navy, have served to provide a basis for many later developments in aviation medicine and physiology.

## DEFINITIONS AND ETIOLOGIC CLASSIFICATIONS OF DYSBARISM

There have been many terms applied to the individual symptoms and the symptom complex which occur when humans are exposed to alterations of barometric pressure. The first terms were used in connection with divers and caisson workers. Because the symptoms were noted to occur on decompression, the syndrome was termed *decompression sickness.* When low pressure chambers came into common use, and when aircraft became capable of attaining high altitudes, some of the terms used in describing divers and caisson workers were also applied to aviators' symptoms.

Since the terminology used at the present time may be confusing, it is best to explain the relationship between commonly used terms and several systems of classification.

### Decompression Sickness

Defined as a syndrome *exclusive of hypoxia and airsickness,* decompression sickness results from a reduction in barometric pressure and is characterized clinically by a variety of symptoms including joint pains (bends); cough, chest pain, and difficulty in breathing (chokes); vertigo (staggers); skin disturbances as rash and paresthesia (the itch); and various central nervous system symptoms such as visual field defects, aphasias, paralyses, etc. Decompression sickness occurs in individuals such as divers who are decompressed from high pressures to normal atmospheric pressure—as in caisson disease (compressed air illness)—and also in flying personnel who are decompressed from sea level pressure to subatmospheric pressure (altitude decompression sickness).

Some authors have used *aero-embolism* as a term synonymous with the above definition of decompression sickness. This definition, however, considers only one category of symptoms. To include other symptoms which occur at altitude, the following classification system is used and has been of tremendous didactic value. According to this classification, decompression sickness is defined as a syndrome, exclusive of hypoxia and airsickness, re-

sulting from a reduction in barometric pressure and characterized clinically by a variety of symptoms caused by two chief mechanisms—*evolution of dissolved gases from solution*, and the *expansion of trapped gases*.

## Symptoms resulting from evolved gases (Henry's law)

1. Bends
2. Chokes
3. Central nervous system symptoms
   a. Paresis
   b. Paralysis
   c. Visual field defects
   d. Aphasias
   e. Confusion, etc.
   f. Sensory losses
   g. Vertigo
4. Skin disturbances
   a. Rash and mottling
   b. Paresthesias
   c. Edema

## Symptoms resulting from trapped gases (Boyle's law)

1. Abdominal distention
2. Effects on the ear
   a. Barotalgia
   b. Barotitis media
   c. Barotitis externa
   d. Barotraumatic deafness

3. Barosinusitis

4. Baromastoiditis

5. Barodontalgia (?); mechanism uncertain

It is pertinent to mention again that these symptoms should be thought of in connection with Henry's law and Boyle's law, and that the pertinent details of the gas laws have been previously considered.

Recently there has been an attempt to formulate a classification which would satisfy objections to the term "decompression sickness." The chief objection to the term "decompression sickness" has been the fact that some of the symptoms included in the definition, such as barotalgia, are *usually* the result of *recompression* which occurs during *descent* from altitude rather than from *decompression* on *ascent* to altitude.

The following classification scheme has been proposed based on the use of a master term *dysbarism* to replace the term *decompression sickness*. Two subdivisions of dysbarism are *hypobarism* and *hyperbarism*.

## Dysbarism

This syndrome, exclusive of hypoxia and airsickness, consists of those disturbances in the body which result from the existence of a pressure differential between the total ambient barometric pressure and the total pressures of dissolved and free gases within the body tissues, fluids, and cavities.

**Hypobarism.** Hypobaric disturbances in the body result from an excess of the gas pressure within the body fluids, tissues, or cavities over the ambient gas pressure. Examples are:

1. Bends
2. Chokes
3. Vertigo (staggers)
4. Central nervous system symptoms

5. Skin disturbances
6. Abdominal distention
7. Barodontalgia (?)

**Hyperbarism.** Hyperbaric disturbances result from an excess of the ambient gas pressure over that within the body fluids, tissues, and cavities. Examples are:

1. *Barotalgia* during *descent* from altitude may occur in an individual whose pharyngeal orifice of the eustachian tube is blocked. This blockage prevents the entrance of air from the oral cavity into the middle ear and results in a differential pressure across the tympanum since the air pressure in the external auditory canal is increasing as the descent is made.

2. *Barosinusitis* pain during *descent* from altitude is not uncommon if a previous sinusitis exists or an acute upper respiratory infection causes impairment of pressure equalization.

NOTE: A malfunction of the valvelike structure at the pharyngeal orifice of the eustachian tube can also cause barotalgia in a diver who is compressed to several atmospheres of pressure. If the orifice is closed so that air cannot enter the middle ear at the same rate that it enters the external auditory canal, then a differential pressure is established.

**Conditions associated with either hypobarism or hyperbarism**

1. Barotalgia
2. Barotitis media
3. Barotitis externa
4. Barotraumatic deafness
5. Barosinusitis
6. Barodontalgia (?)

It is to be noted that although the term *dysbarism* is preferable to that of *decompression sickness*, there is considerable overlap in the classification of a symptom under the subheadings of *hyperbarism* or *hypobarism*. This arises from the fact that the *etiologic*

*mechanism* is such that the symptom may occur either when there is an excess of the ambient gas pressure over that in the body, or an excess of the gas pressure within the body over that in the ambient atmosphere. For example, barotalgia most frequently is a hyperbaric symptom; that is, the condition usually occurs on *descent* from altitude or in compression of a diver. If the pharyngeal orifice of the eustachian tube is blocked, however, and does not allow air to escape from the middle ear during *ascent* to altitude, then a differential pressure across the tympanum also results since the pressure in the middle ear will be greater than that in the external auditory canal. Pain in the ear occurs, regardless of the exact mechanism, since in both cases the eardrum is affected. The mechanism of the above symptoms is discussed more fully in separate sections.

**Caisson Disease**

Caisson disease usually refers to the syndrome produced in caisson workers as a result of decompression from higher to lower pressures, the latter of which is atmospheric or greater. This term is not applicable to aviation medicine. It is notable, also, that although the chief symptoms of caisson disease—such as bends, chokes, etc.—are hypobaric phenomena, the symptom of barotalgia is most common on *compression* and is, therefore, due to hyperbarism.

**Aero-embolism**

In aviation medicine, this term refers to hypobaric phenomena in which gas bubbles are formed in the blood stream.

**Aero-emphysema**

In aviation medicine, this term refers to hypobaric phenomena in which gas bubbles are formed in the tissues.

**Pompholyx—A Bubble**

The terms *pompholyembolism* and *pompholyemphysema* could be used instead of *aero-embolism* and *aero-emphysema*, respectively. Actually, they are more accurate because the term "aero"

implies that the bubble has the composition of air, which, as we shall see later, probably is untrue. However, these more correct terms have the obvious disadvantage of being unwieldy in aeromedical reporting.

## THEORIES OF ETIOLOGY OF ALTITUDE DYSBARISM

There are two main mechanisms which have been postulated to explain such features of altitude dysbarism as bends, chokes, and symptoms of central nervous system origin. For discussion of the older theories concerning the etiology of symptoms due to dysbarism occurring on exposure to high atmospheric pressures, see Hill (129, ch. 7). These mechanisms are: (1) changes in the circulation; (2) formation of bubbles. As we shall note, there are differences of opinion concerning the initial phase of the mechanism, and there may be considerable overlap in various phases since bubbles can also cause alterations in the circulation.

### Changes in Circulation

**Intravascular agglutination theory.** Swindle (233) noted the presence of nongaseous emboli in the form of a fragile coagulum which occluded the blood vessels of animals exposed to altitude. These fine networks were believed to be due to plasma flocculation. When a clump of this kind was found to occlude a vessel, the injection of India ink showed that the coagulum was capable of acting as an embolus because the ink did not stain the areas peripheral to the occluding meshwork. Possibly, there was an aggregation of erythrocytes in the network (212). There was also some evidence quoted by Swindle (233) that agglutination of this type could be an important factor in causing the symptoms of decompression in divers. According to Swindle, paroxysmal muscle contraction initiates agglutination. This would correlate with exacerbation of bends by exercise. Also, individual differences in agglutination are common and provide a logical explanation for differences in susceptibility to decompression sickness. Knisely (159), however, who is very familiar with in vivo technics of observing the circulating blood of human subjects,

states that he had never seen decompression to initiate intravascular agglutination or to cause an increase in a mild agglutination which was already present.

Jacobs and Stewart (145) exposed albino rats to positive pressures from which they were rapidly decompressed. They found no clear evidence of rouleaux formation of erythrocytes and no increase in sedimentation rate which should be a function of agglutination. They did observe the blood platelets to form aggregates about small gas bubbles and later to appear as free aggregates in the blood. It was suggested that such aggregates of platelets with or without addition of fibrin could conceivably lead to occlusion of small vessels in certain regions of the body. Gersh and Catchpole (87), who used a freezing and drying technic which should have demonstrated aggregates and flocculates, failed to find such changes in animals undergoing decompression.

**Angiospasm theory.** Knisely (159) observed directly the scleral vessels of human subjects at altitude with a binocular-dissecting microscope using strong cross-illumination. He saw no bubbles in these scleral vessels, but did observe arteriospasm in all individuals above 30,000 feet which, in the ones with overt bends pain, was sufficient to obliterate arteries. Return to ground level resulted in the return of normal-sized vessels in a variable period of time. Beginning at 20,000 feet there are increasingly prolonged spasms of a progressively larger and larger number of arterioles, particularly in connective tissues and muscles (158).

Prolonged arteriolar spasm was seen in every case in the 20 subjects studied (159) where symptoms of bends or chokes occurred. Some of the subjects showed various degrees of constriction of the venules. Subjects with bends pain have had a noticeably slower refilling of the nail beds than subjects at altitude without pain. Some have had nails remain white for several minutes. Knisely interprets this as meaning that arteriolar vasoconstriction is present because, since the venules have valves, there is no backflow and, hence, the time it takes for a nail to become pink is a rough indication of the total rate of flow through arterioles supplying the nail bed. Parallel to the "nail bed filling

time" is the "arm-vein refilling test" in which a subject at altitude holds his arm up vertically until the veins are collapsed. The arm is then held down vertically and the time noted for the great veins of the hand and forearm to refill. The valves of the veins prevent backflow so that the filling time is a rough indicator of the total flow rate through the arterioles toward the end of the extremity. Subjects with bends pain had a noticeably slower refilling time than subjects without pain. Knisely believes that the lowering of temperature in the extremities and the slow refilling of nail beds and arm veins indicates that bends phenomena are associated with vascular phenomena.

Reduced rates of blood flow through tissues can produce hypoxia, and contractions of hypoxic muscles can produce pain. It is also possible that reduced rates of blood flow through tissues may permit gas to accumulate and the bubbles developed in or beside small vessels can obstruct the flow further. In an attempt to decrease the blood flow through an extremity while at altitude, Knisely et al. (160) had each of 36 subjects hold an extremity in a vertical position. Elevation of an extremity either initiated the pain or, if the pain was already present, made the pain more severe. These results are in contrast to those in subjects who were given aminophylline where elevation of the part usually did not result in pain (158, 161).

One group of 65 subjects was exposed to 38,000 feet until symptoms of bends were developed (158). They then descended to 20,000 feet, and the pain was alleviated. The pains promptly reappeared on decompression to 38,000 feet. In none of these subjects did the pain fail to reappear. A second group of 41 subjects was taken to 38,000 feet and exercised until they experienced fairly severe symptoms of bends. Recompression to 20,000 feet was effected and aminophylline given intravenously after which ascent to 38,000 feet was again made. Of the 41 subjects, 12 were free of symptoms and 5 had a return of mild symptoms which later disappeared. The seemingly important point was that, frequently, the recurrence of pain could be relieved by exercise of the affected limb.

That circulatory effects are associated with bends symptoms is indicated by a number of other investigations. Evelyn (71) noted that occasionally the joint affected by bends seemed to be colder than the corresponding opposite joint. Stewart et al. (230) noted that, in most of the instances recorded, the hand temperature of a limb affected by bends was lower than in the other hand. Fulton, quoted by Knisely et al. (160), reported that the pulse volume of the fingers of subjects exposed to low pressures has been found decreased in the majority of flights. This decrease often develops some time before bends pain becomes evident which indicates that the peripheral circulation is markedly diminished by ascents to high altitude. Tobias et al. (242-244) showed that in subjects exposed to an altitude of 38,000 feet there was usually a slow, gradual drop in skin temperature. The temperature fall is usually faster in individuals who develop decompression sickness. Of 18 subjects with the highest hand temperature, only 2 were forced to descend because of incapacitating symptoms. Of 18 subjects having the lowest hand temperatures, 13 were forced to descend (243). Kaufman et al. (155) concluded from 66 man-flights to 38,000 feet that digital blood flow, as measured by an impedance technic, is sensitive to decompression to that altitude. The least reduction in digital blood flow was observed in subjects who sat quietly at rest at 38,000 feet. The greatest reduction was observed in subjects who exercised at altitude and who had not previously denitrogenated. If the subjects denitrogenated at ground level for 30 minutes before ascent to 38,000 feet and then exercised at that altitude, there was a reduction of digital blood flow comparable to the tests in which they sat quietly. It was also recorded by these authors that the reduction in blood flow often occurs before any other signs of decompression sickness appear, and that there was good correlation in the extent of the reduction of digital flow and the duration of time the subject tolerated the altitude. Under all the procedures studied, the digital blood flow was reduced sharply in the first 30 minutes at 38,000 feet with further reduction being effected up to the 100-minute point, at which time the experiment was terminated. Descent to ground level did not effect an immediate return to normal digital flow values, but the average recovery was fairly prompt. Lazarow et al. (165) noted the vasoconstriction in frogs at high altitude

and decreased rates of blood flow through tissues although no bubbles were seen. Since the animals were anesthetized the vasoconstriction could not be attributed to pain. Vasoconstriction which occurred at altitude in rabbits and goats was not considered to be related to bubble formation in another series of tests (194).

One difficulty in studying the mechanism of bends has been occasioned by the fact that small animals are relatively refractory to bubble formation. The reason for this is probably a matter of a faster circulation and a larger circulatory bed resulting in better denitrogenation. Air can be injected into the nutrient artery of the bone or into the medullary cavity of bone in a dog, but no bubbles will be seen by x-ray at ground level. In a series of experiments (144), 5 cc. of air were injected into the femoral artery of 10 dogs. No gas was seen by x-ray at ground level. Within 5 minutes the animals were taken to 40,000 feet and the gas had expanded sufficiently to be visualized in the veins. Most important is the fact that 4 animals died as a result of pulmonary embolism.

The circulation problem may have been partially resolved by the introduction of a technic recently reported by Ivy and Wedral (144). In attempting to study bubble formation in dogs, they have theorized that one method of promoting bubble formation would be to reduce the blood pressure for extended intervals of time. This has been accomplished by the administration of Witte's peptone in amounts sufficient to keep the blood pressure at a low level. Exposure of the treated animals to altitude has resulted in the uniform production of bubbles. This method, or modifications thereof, promises to help elucidate the mechanism of bends, chokes, and perhaps central nervous system disturbances. Even if the technic were complicated by numerous questions concerning the other possible actions of Witte's peptone besides lowering the blood pressure, valuable information should be forthcoming.

There are at least several lines of indirect evidence that angiospasm may be the cause of symptoms at altitude which appear to be of central nervous system origin. First is the matter of delayed reactions which may occur after exposures to altitude.

Presumably, the bubbles have redissolved by that time and, certainly, the use of the angiospasm theory to explain temporary visual defects, paresis, and paralysis is attractive because it is well known that reflex autonomic nervous system effects may cause severe angiospasms which endure for considerable lengths of time. In this connection, the syndrome of scotoma and headache was explained by reflex vascular changes in one series of experiments (67). Concepts of angiospasm in this latter category will be discussed more fully in the special report on "Neurocirculatory Collapse at Altitude" (by H. F. Adler, USAF School of Aviation Medicine, June 1950).

Blood sludging caused by ischemic hypoxia due to vascular occlusion by gas bubbles may be a part of the mechanism of bends pain (66, 233, 248). As mentioned previously, vasoconstriction may be an important part of the mechanism. It has been noted to occur in frogs (165, 195) and man (160), although Reed and Blinks (195) did not believe that the vasoconstriction was related to bubble formation and Patek et al. (186) noted sludging of blood in cats but did not report vasoconstriction.

Smith and Manning (219) made a cardiovascular study of 6 subjects exposed seven times to 35,000 feet for 3 hours. The electrocardiograms of the 2 most susceptible subjects showed some lengthening of the P-R interval following the exposures, and the most susceptible subject showed a marked lowering of the T-wave which may have been due to hypoxia. No other changes were noted. These findings could be significant since they correlate a labile cardiovascular system with symptoms of dysbarism.

If the pain of bends may be compared to the pathologic type of pain which occurs when local circulatory changes produce ischemia, then, according to the concepts of Lewis (167), local chemical substances may be elaborated by the injured tissues and produce pain. The chemical nature of the local substances produced is unknown, but along with the concept of a "pain substance" it has been postulated that local changes in injured tissue may result in a decreased threshold of nerves for pain (166). Further, the local tissue change through axon and other reflexes

may possibly cause hyperalgesia of large areas supplied by other branches of the nerve trunk. Thus, the effect of an initial stimulus in a small region may be that of producing pain referred to a much larger area. Because individuals differ in their pain tolerance, it could be postulated that the matter of "biochemical individuality" determines the amount of "pain substance" produced or its quantitative or qualitative effects.

**Electrolyte shift theory.** Larkin and Watts (162) proposed a theory which ascribed bends to a shift of electrolytes in the body so that water was also shifted to the intercellular fluid. This, in effect, produced a syndrome similar to surgical shock and also similar to the mechanisms producing "miner's cramps" when ions are lost and water shifts into the tissues. Investigation of the actual blood chemistry was not performed in the subjects exposed to altitude. In an attempt to prevent a shift of electrolytes, subjects were exposed to 35,000 feet for 90 minutes with a standard exercise after a 7- to 10-day period in which calcium lactate, vitamins A and D, and 7.5 gm. of NaCl were given in addition to regular foods. According to the data, there was an increased resistance to bends in this group of tests as compared to the controls. They also reported that 2 subjects who usually drank large quantities of milk were the most resistant subjects to bends that they had ever seen. The studies by Warwick (249, 250) could be interpreted to support the electrolyte theory. By forcing fluids on 2 subjects who were highly susceptible to bends at 35,000 feet, one showed a marked increase in resistance to bends for 5 days while the second subject demonstrated a lesser degree of protection. When 2 subjects who were highly resistant to bends voluntarily restricted their fluid intake for 6 days there was a progressive increase in susceptibility to bends which disappeared when normal fluid intake was again permitted. On the basis of 17 subjects who made chamber ascents, on 14 consecutive days, to 35,000 feet for 3 hours, Warwick (249) found that the incidence of symptoms was significantly higher in those who had low urine outputs as compared with those with high urine outputs.

The above tests by Larkin and Watts were duplicated at 38,000 feet for 2 hours with a similar exercise on 7 individuals who

had been repeatedly exposed to altitude (143). The incidence of bends was well known in these subjects since they had served as subjects on many types of experiments. The results of the tests with the salts and milk in these subjects showed no significant decrease in bends symptoms. If anything, the incidence was slightly increased. In summary, it may be indicated that the crucial blood studies and differentiation of various factors which are concerned with bends have not been studied adequately enough to completely void the idea that electrolyte changes do occur and contribute to some of the manifestations of altitude dysbarism. In this connection, collapse at altitude or after descent from altitude may be attended by a shock syndrome. Electrolyte alteration could be a factor in these instances.

**Formation of Bubbles**

The greatest amount of evidence has accumulated in favor of bubbles being a primary cause of such manifestations of dysbarism as bends, chokes, vertigo, central nervous system symptoms, and skin disturbances. Since this theory has the most support, we shall examine its various aspects in considerable detail.

**Parallelism between bubbles and symptoms.** In general, there is a significant relationship between the symptoms of dysbarism and the presence of bubbles as seen by x-ray (43, 70-72, 94, 238, 252). In man, the higher the altitude attained, the greater the incidence of bends, chokes, etc. Correlated with this is the fact that more and larger bubbles are noted in both man and animals when decompression is effected to very high altitudes as compared to lower altitudes. Also, in caisson disease, the greater the differential pressure range through which decompression takes place, the more bubbles formed and the more severe are the symptoms. In man, exercise at altitude greatly increases the incidence of bends and chokes. In animals, it has been shown that exercise at altitude may greatly stimulate the formation of bubbles (177, 254, 255).

Obese individuals are more susceptible to bends symptoms at altitude and also to caisson disease. In correlation, nitrogen is about 5.3 times more soluble in fatty tissues than in other body fluids such as blood (25, 34).

In man, denitrogenation by breathing 100% oxygen before ascent to altitude is highly protective against altitude bends and chokes; and in animals, denitrogenation reduces bubble formation Likewise, denitrogenation protects against caisson disease.

The bubble theory explains the effectiveness of recompression in the treatment of bends in caisson disease in divers. It also explains the effectiveness of descent from high altitude in relieving symptoms of dysbarism in aviators. In both instances, the bubble size is reduced and symptoms usually relieved.

A definite correlation has been found between the incidence of caisson disease and the theoretic saturation of tissues with nitrogen (213). In this connection it should be remembered that when the caisson worker is subjected to increased pressures for short periods, the amount of dissolved nitrogen in his body is far less than that which he would have if equilibrium were attained. It may take several hours for the less accessible tissues and cerebrospinal fluid to become completely saturated and in equilibrium with the increased pressure of his environment. On some occasions bubbles can actually be palpated in the skin and be caused to move by exertion of pressure.

**Discrepancies in the bubble theory.** Several questions have been raised as to whether the occurrence of bubbles explains the observed phenomena adequately. If symptoms are caused by bubbles, then an explanation is needed as to why there may be a considerable delay in the appearance of symptoms when the minimum altitudes for bubble formation are attained (233), and why some symptoms may persist long after descent. In some instances, bends has been absent at the peak altitude but was experienced during descent (203).

Subjects at altitude have experienced bends in an extremity when no definite bubbles could be visualized by the roentgenographic technic. Conversely, x-ray sometimes demonstrates the presence of large collections of gas bubbles even when the subject shows no symptoms of bends (43, 252).

Differences in susceptibility to bends between different individuals, and even in the same individual on separate exposures, are often very marked. This fact is difficult to explain on the basis of the amount of nitrogen dissolved in the body, differences in the rate of nitrogen elimination, circulation factors, etc.

The difficulty of demonstrating absolutely that bends, chokes, and central nervous system symptoms are caused by bubbles is one which arises from the lack of suitable technics applicable to man. It is possible to explain many of the apparent discrepancies, but obtaining the actual proof of the etiologic mechanism in any single instance would be a formidable task. With our present knowledge we can only indicate that a combination of the bubble and angiospasm mechanisms offers a sufficient theoretic basis for explaining most of the phenomena. For example, in the instance of delayed appearance of symptoms, several lines of evidence may be cited. When rats were rapidly decompressed from several atmospheres of pressure to 1 atmosphere, the increase in size of bubbles progressed during the first hour after decompression to the point where the blood eventually became a froth (145). This mechanism could explain the delayed symptoms occurring in humans at altitude, but whether it operates in this case is uncertain. As mentioned previously, angiospasm—either occurring alone, in conjunction with, or as a result of bubbles—may explain any delay of symptoms, depending upon the location and degree of ischemia. However, if angiospasm alone is responsible and bubbles are not a part of the etiologic mechanism, it is difficult to see why denitrogenation is so effective in preventing bends and chokes and why recompression is so immediately effective in the treatment of caisson disease.

In a few instances, bends was absent at the peak altitude but was experienced during descent (203). This unusual phenomenon may reasonably be explained by postulating that, as the descent took place, the bubbles, whether intravascular or extravascular, became smaller. As they decreased in size, they could have moved with greater ease to a different and more sensitive area and produced the pain. In several x-ray studies some individuals had bends in locations where no bubbles were readily evident and others

manifested no bends symptoms in areas which showed large collections of gas (43, 70, 85, 238). These findings may be interpreted as meaning that a small bubble in a "critical focus" or very sensitive area could produce severe symptoms, whereas larger bubbles in less sensitive foci may produce few or no symptoms. Further, the absence of detectable collections of gas by the x-ray technic does not necessarily mean that small bubbles could not be present. Obviously, angiospasm with ischemic pain could also explain the phenomena and similarly would remain undetected by roentgenograms unless special vessel-visualizing technics were used. If angiospasm and the resulting ischemia were primarily responsible for the pain, however, some further explanation may be necessary to account for the findings in several series of tests at altitude that pressure, as by arterial tourniquet, hydrostatic pressure, etc., will temporarily alleviate the pain of bends (10, 80).

**Physical and physiologic aspects.** When a gas is in contact with a liquid, the tension of dissolved gas is directly proportional to the partial pressure of the gas over the liquid. If the partial pressure of the gas over the liquid is *slowly* reduced, the gas will *slowly* diffuse out of the liquid so that the tension of gas in the liquid tends to remain in equilibrium with the partial pressure of the free gas above. If the partial pressure of the gas is *reduced suddenly*, the pressure of dissolved gas in the medium exceeds the tension of gas with which it is in equilibrium and the solution is supersaturated. When the tension of dissolved gas equals or exceeds the barometric pressure, bubbling can occur theoretically. Expressed algebraically, bubbling can occur when:

$$\text{Tension of gas (t)} = \text{Barometric pressure (B)}$$

Dividing both sides of the equation by B, we obtain a ratio which states that bubbling can occur when the gas tension divided by the barometric pressure is equal to or greater than 1.

$$\text{(t) Gas} = \text{B}$$

$$\frac{\text{(t) Gas}}{\text{B}} = \frac{\text{(B)}}{\text{(B)}} = 1 \text{ or } > 1$$

Applying this equation to nitrogen, we consider that the tension of nitrogen in the body at sea level is about 570 mm. Hg in arterial blood, for example; hence,

$$\frac{570}{B} = 1, \text{ and, } B = 570 \text{ mm. Hg}$$

Thus, when B equals 570 mm. Hg, which is equivalent to about 7,744 feet pressure altitude, the body nitrogen tension is equal to the barometric pressure and, *theoretically* at least, bubbling can take place. Actually, bubbles are not seen at these low altitudes, especially in small animals. In man, bubbles have been shown to be present by x-ray at all altitudes above 20,000 feet (70-72). This implies that before bubbling occurs, the nitrogen tension must equal the barometric pressure plus some factor *X*; that is, X represents unknown factors which prevent bubbling. This may be expressed algebraically as follows:

$$p\,\text{Gas} = B + X$$

Dividing both sides of the equation by B + X we get an equation called the critical ratio for bubble formation.

$$\frac{p\,\text{Gas}}{B + X} = \frac{B + X}{B + X}$$

$$\frac{p\,\text{Gas}}{B + X} = 1 \text{ or } > 1 = \text{critical ratio}$$

It will be noted that we have referred to nitrogen gas as being chiefly concerned with bubble formation because it is the gas which has the greatest tension. Nitrogen gas is considered inert and does not enter into metabolism as do carbon dioxide and oxygen and, hence, cannot be disposed of easily under some conditions.

Since carbon dioxide has a tension in venous blood of about 47 mm. Hg, it theoretically would not bubble below approximately 63,000 feet. The tension of carbon dioxide in local tissues may be higher than 47 mm. Hg and this factor could influence bubble growth locally.

Considered separately, water at body temperature having a vapor tension of 47 mm. Hg would not boil below 63,000 feet, and venous or tissue oxygen having a lower tension would probably not bubble below 67,000 feet in a local region where its tension is about 40 mm. Hg. However, once bubbles of any type are formed, their composition could be greatly altered by the diffusion of various gases into them, and this probably happens, especially in bubbles produced at altitude.

Concepts of bubble formation are given for orientation and to emphasize that gas tensions do play an important role in bubble formation. However, the mechanism as given is far too simple. A compilation of some of the more recent studies which have contributed to our knowledge of bubble formation will serve to present a better analysis of the problem.

There are a number of physical and physiologic factors which will govern bubble formation during decompression. In a series of papers (117-122, 176, 257), Harvey and associates have discussed these factors in detail.

The complexity of the problem can only be realized by a perusal of their reports and those of a number of other investigators (49, 52, 85, 87, 88, 165, 194). Some of this work has been summarized by Catchpole and Gersh (50). In the present discussion we wish only to present some of the more positive considerations.

By using an equation introduced by Harvey et al. (119), which considers the factor of hydrostatic pressure in addition to gas tensions, we may expand the concept concerning the tendency of gases to bubble and leave the liquid phase. This equation is:

$$\Delta P = t - P$$

in which

$\Delta P$ = the differential pressure or tendency for gas to leave the liquid phase

$t$ = total tension of gas in the medium

$P$ = the absolute pressure (i.e., the total pressures of gases in the body plus the hydrostatic pressure)

*Arterial $\Delta P$ at Sea Level.* In the above equation, $t$ would have a value of 760 mm. Hg at sea level, and the absolute pressure ($P$) in this artery at sea level, if we assume an arterial blood pressure of 125 mm. Hg, would be 760 + 125 = 885 mm. Hg. Therefore, the equation would read:

$$\Delta P = 760 - (760 + 125)$$

$$\Delta P = -125 \text{ mm. Hg}$$

*Great Vein $\Delta P$ at Sea Level.* If we assume for simplicity that the value of $t$ for venous blood is 760 mm. Hg and if we consider the blood pressure of a great vein in the chest to be 0 mm. Hg, then:

$$\Delta P = 760 - (760 + 0)$$

$$\Delta P = 0$$

As can be seen in the above equations, $\Delta P$ in the artery at sea level is negative. This means that there is no tendency toward bubbling, and the blood pressure of 125 mm. Hg may be thought of as a hydrostatic pressure helping to keep gas in solution.

At sea level, the $\Delta P$ of a large vein approaches zero. The same would also be true of tissues.

In the equation $\Delta P = t - P$ the important concept to keep in mind is that, as the differential pressure ($\Delta P$) becomes positive, there will be an increased tendency for gas to leave a liquid and form bubbles. The differential pressure can be caused to approach zero or become positive, thus favoring bubble formation by:

1. Increasing the value of $t$.
2. Decreasing the 760 mm. Hg total pressure of gases on the body.
3. Decreasing the hydrostatic pressure.

Let is examine each of these three factors to give some idea of what the differential pressure could be if the individual factors varied.

## Gas tension (t)

Suppose that in a local region of the body, as in fatty tissue, the tension of gas (t) remains high (760 mm. Hg) while the total pressure to which the body is exposed is reduced. The tension of gas in fatty tissue with a poor circulation would have a tendency to remain high. The result would be a shift of $\Delta P$ toward zero and a promotion of bubble formation. The value of $t$ can be increased locally by the local production of carbon dioxide, as in muscular exercise, and a high local $P_{CO_2}$ would rapidly increase the size of any bubble which was formed because of its rapid diffusion and high solubility characteristics (50, 119). The local tension of gas (t) would tend to remain high during very rapid ascents to altitude.

## Absolute pressure

As indicated above, the absolute pressure (P) consists of two components: *the total pressure of gases* (760 mm. Hg at sea level) and the *hydrostatic pressure* in the artery, vein, or tissue.

The total gas pressure on the body and, hence, in the body, can be reduced by ascent to altitude. For example, on very rapid ascent to 5,000 feet (about 635 mm. Hg) the differential pressure ($\Delta P$) in an artery with a hydrostatic pressure of 125 mm. would be approximately zero, whereas $\Delta P$ in a large vein with a hydrostatic pressure of 0 mm. Hg would be positive.

$$\text{Artery } \Delta P = 760 - (635 + 125) = 0$$

$$\text{Vein } \Delta P = 760 - (635 + 0) = +125$$

This means that at this altitude, and according to this theoretic treatment, there would be little tendency for bubbles to form in arteries, but there would be a possibility for bubbling in veins and tissues.

As before, however, there is no evidence of bubbling at these low altitudes and many factors must be considered. One of these factors is the rapidity with which various tissues reach gaseous equilibrium with the ambient atmospheric pressure.

Arterial blood, for example, rapidly reaches equilibrium with alveolar air. Because of this fact it was necessary to postulate that "very rapid ascent" was made to 7,744 feet (the value used in the first simplified analysis) since, if the ascent were made slowly, the $t$ value of gas in arterial blood would have time to fall just as the total pressure factor of $P$ were falling and, hence, the differential pressure would not approach zero. In the section on denitrogenation we shall see that the blood stream exchanges gases very rapidly as compared to other tissues. Obviously, however, if the value of $t$ in fatty tissue remains high because of poor gas exchange, then on ascent to altitude bubble formation will be facilitated in fatty tissues as compared to arterial blood, venous blood, or other tissues with less fat and better circulation.

Until now we have discussed only hydrostatic pressure of +125 mm. Hg and 0 mm. Hg. It has been indicated also that a decreased hydrostatic pressure causes the differential pressure ($\Delta P$) to approach zero; this favors bubble formation. In addition, however, there are instances when the hydrostatic pressure may be lowered rather quickly in a local region by increases in mechanical tensions (117). During muscle contractions, for example, local mechanical tensions may develop. Relatively small "pulls" on a hydrophobic surface in a very small area can produce a relatively great mechanical tension which reduces the hydrostatic pressure factor and causes the differential pressure not only to approach zero but also to become positive. These local mechanical tensions developed in muscles may be likened to the action of a "suction cup" in producing a local area of greatly reduced pressure. Under these conditions, bubbles could easily be formed locally in muscles which were being exercised.

We must realize also that the differential pressure ($\Delta P$) can be theoretically calculated for a local area, for the entire body $\Delta P$ really represents a complicated aggregate of the various differential pressures which exist in the local regions.

As a further note of caution, we need only point out that in order to present the information as simply as possible, the differential pressure ($\Delta P$) in the preceding discussion has been shown

to be affected by only a few factors. Actually, in physical systems, such factors as Reynolds's cavitation, contact angles between bubbles and hydrophilic and hydrophobic surfaces, pressure pulses, sound waves, Bernoulli effects, turbulence, suprasonics, etc., may be or are important in bubble formation (117). In physiologic systems, stretching, cutting, and acute crushing of tissue alters mechanical tensions and, hence, changes the hydrostatic factor of *P*. Similarly, blood flow and, thus, gas exchange, as affected by vasoconstriction and vasodilatation in local areas, may exert their particular effects on the tendency of a tissue to form bubbles.

**Size and composition of bubbles.** It is generally accepted that it is more dangerous for the diver or caisson worker to be decompressed from 5 atmospheres of pressure (3,800 mm. Hg) to 1 atmosphere (760 mm. Hg) than for the aviator to be decompressed from 1 to ⅕ atmosphere (152 mm. Hg). Although some of the reasons for this fact would seem to be obvious, others need discussion.

As first consideration, we can show by formula that *bubble volume* will be the same when the individual is decompressed from 5 atmospheres to 1, as it would be on decompression from 1 to ⅕ atmosphere.

$$V_2 = \frac{P_1 V_1}{P_2}$$

in which

$V_2$ = the final volume

$P_1$ = the initial pressure

$V_1$ = the initial volume

$P_2$ = the final pressure

In the case of the bubbie formed on decompression *from 5 atmospheres to 1 atmosphere:*

$$V_2 = \frac{3800 \cdot V_1}{760} = 5 \text{ times } V_1$$

which shows that the bubble volume ($V_2$) will have increased five times.

In the case of the bubble formed on decompression *from 1 to ⅕ atmosphere:*

$$V_2 = \frac{760 \cdot V_1}{152} = 5 \text{ times } V_1$$

which also shows that the bubble volume ($V_2$) will have increased five times.

At this point it should be indicated that it is the *bubble volume* which will produce the pathologic effects; hence, if the bubble volume in the two instances is the same, then we must seek further for an answer to the question as to why decompression is more dangerous in the case of diver or caisson worker than in the aviator.

There are probably several possible explanations. More bubbles are formed on decompression from high pressures (120, 188). The number of bubbles per unit volume of fatty tissue increases as animals are decompressed from greater and greater pressures (88). It is also true that even though the volumes may be the same, the weight of each bubble formed in the case of the diver is much greater, since by weight he has about five times as many molecules in each bubble. The reason why the individual decompressed from 5 atmospheres would have more bubbles is that in order for a bubble to be stable it has to have a critical radius and a certain number of molecules (183). In the case of the diver, the theoretic critical radius and number of molecules necessary to form a stable bubble is less than for the aviator. Since the diver has more molecules of gas in solution, it is more likely that sufficient molecules will congregate to form bubbles than in the aviator where more molecules have to assemble from a larger field which is less densely populated. Piccard (188) calculated that the individual being decompressed from 5 atmospheres to 1 forced a bubble when 27.6 million gas molecules met, whereas the number necessary on decompression from 1 to ⅕ atmospheres is 690 million.

A second important factor may be that the bubble formed in the case of the diver consists chiefly of nitrogen, which is high in both percentage and tension. It is relatively difficult for the body to get rid of nitrogen because it is an inert gas; therefore, the stability of the bubble is probably increased. In experiments on cats (182) it was shown that the intravenous injection of air produced far more stable gaseous emboli than oxygen injected by the same route. In comparison, the bubble formed at altitude will be chiefly composed finally of gases other than nitrogen, and the body can more easily dispose of the oxygen and carbon dioxide fractions since they are metabolic gases.

In addition to these factors, several important circumstances operate to make altitude dysbarism less dangerous than diver's or caisson disease. Altitude dysbarism is *alleviated by descent from altitude*, whereas in diver's and in caisson disease, symptoms are *produced by ascent to sea level pressures.* In other words, the symptoms of altitude dysbarism are ameliorated when the individual returns to his habitual environment, whereas the divers' and caisson workers' symptoms are produced when they attempt to return to their habitual environment. The latter individuals are likely to avoid treatment if they believe the symptoms are mild and, hence, are prone to suffer more severe and even permanent damage because of their unwillingness to spend several hours to be recompressed and then decompressed slowly. Undoubtedly, this has contributed to the larger number of more serious reactions on decompression. As Behnke (26) indicated, central nervous system symptoms, as of the spinal cord, are *rare in ascents to altitude* and there is a rapid amelioration of symptoms when descent is effected. This is not true of caisson workers where *pathology in the spinal cord and brain are common* (129).

**Bubbles in altitude dysbarism.** The first consideration in bubble formation is to assume the existence of "gas nuclei" because, for bubbles to form *de novo*, a differential pressure of 100 to 1,000 atmospheres is needed. However, at a hydrophobic surface, bubbles can form *de novo* under certain conditions of locally produced, very large differential pressures caused by changes in mechanical

tension. The gas nuclei are thought to be located in blood vessels (122), especially on the walls, and these nuclei are probably present or formed on the surface of cells rather than in liquid (117).

The second consideration in bubble formation is that when such gas nuclei are present, the differential encountered at altitude could produce bubbles. In theory and in fatty tissues, the initial bubbles formed at altitude would mainly consist of nitrogen. Armstrong (12) showed in goats that the composition of the bubbles in venous blood did not show as much nitrogen as was generally accepted in theoretic calculations. In blood from the jugular vein, the bubbles he found had 6.7% oxygen, 28.3% carbon dioxide, and 65.0% nitrogen. In the right ventricle of the heart, the analysis revealed 11.4% oxygen, 28.3% carbon dioxide, and 60.3% nitrogen.

As a third consideration, if we examine the above analysis in the light of present-day thought on the composition of bubbles, it may be said that they, too, may represent only a momentary percentage composition. Once a gas nucleus is present in any area, then the composition of a bubble will depend largely upon the gases in close proximity. Carbon dioxide has been considered as a special facilitator of bubble formation (116, 177), not so much because of rapid diffusion, but owing to its high solubility characteristics. In any local tissue, the tension of carbon dioxide may be only slightly higher than 47 mm. Hg, but the total amount present may be considerable. It may be the chief constituent of a bubble in a local area. If this bubble then moves to a carbon dioxide-poor, nitrogen-rich region, carbon dioxide will diffuse out and nitrogen diffuse in, leaving the bubble composed chiefly of nitrogen. However, because carbon dioxide is diffusible and soluble, it may in any local region cause a bubble to enlarge in size very rapidly. This was demonstrated in a model (117) which consisted of layers of water, each layer alternately saturated with air or carbon dioxide at 1 atmosphere of pressure. When small bubbles moved from the air stratum, they rapidly increased in size on reaching the carbon dioxide layer and just as rapidly decreased in size as they passed into a new region of air-saturated water. It should be made clear that under most conditions, carbon dioxide

merely contributes to the growth of bubbles already formed. This point is stressed because the fact remains that denitrogenation of the body, as by breathing 100% oxygen, reduces bubble formation by reducing the $P_{N_2}$. There is no significant change in the values of carbon dioxide in the various tissues since this gas is being produced metabolically and, in local areas of muscular activity, is being produced in relatively large quantities, thus favoring the growth of bubbles in such regions. From this it should be obvious that the composition of bubbles may change very easily. It would be safe to say that they would contain variable amounts of *oxygen*, *nitrogen*, *carbon dioxide*, and *water vapor*, depending upon the amounts of these gases at the site of bubble growth and the amounts in any new region to which the bubble migrates. The bubble will contain water vapor because, at body temperature, the water vapor would have a pressure of 47 mm. Hg and would be present in all regions of the body.

As an example of this, let us assume that a gas nucleus is present in a local region of the body at 38,400 feet (152 mm. Hg). Let us further assume that the bubble *at first* is composed of pure nitrogen; hence, initially, the bubble has a nitrogen tension of 152 mm. Hg. If we disregard the hydrostatic pressure and other factors and consider only the theoretic tissue tensions of water vapor, carbon dioxide, and oxygen, besides nitrogen, then we may say that into this pure nitrogen bubble will come:

| | | |
|---|---|---|
| $H_2O$ vapor (mm. Hg) | = | 47/152 = 31% by volume |
| $CO_2$ (mm. Hg) | = | 40/152 = 26.3% by volume |
| $O_2$ (mm. Hg) | = | 40/152 = 26.3% by volume |
| Subtotal | = | 127/152 = 83.6% by volume |
| $N_2$ (mm. Hg) | = | 25/152 = 16.4% by volume at equilibrium |

The conclusion is that in this local region the bubble will be composed mainly of *gases other than nitrogen when equilibrium takes place.* If the bubble moved to other regions locally rich in carbon dioxide, then this gas especially would quickly diffuse into the bubbles altering the composition.

**Bubbles in caisson disease.** It is of interest to examine the theoretic differences between bubbles formed at altitude and those formed during decompressions from high pressures. When an individual is exposed to 5 atmospheres of air pressure, his ambient environmental pressure will be $5 \times 760 = 3{,}800$ mm. Hg. The blood and tissues may require about an hour to saturate with nitrogen according to Dalton's law (130). Carbon dioxide tensions, however, are a special problem for several reasons. The first is that when the $Po_2$ is very high, there may be interference with carbon dioxide transport by the hemoglobin, and carbon dioxide may accumulate locally in tissues. This concept will be further expanded in a section dealing with the toxic effects of oxygen. The second reason is that the $Pco_2$ will be prevented from getting too high in the body because a high $Pco_2$ in arterial blood stimulates respiration until it is reduced. Further, even under the increased pressure of 3,800 mm. Hg, the small percentage (0.03%) of carbon dioxide in inspired air would result in very little increase of its tension. The only time carbon dioxide is a factor in any discomforts experienced by divers or caisson workers is when the ventilation of the helmet or chamber is so poor that the carbon dioxide in expired air accumulates (26).

There is little question, however, that the amount of nitrogen and oxygen dissolved in the blood and tissues will be increased when these gases are dissolved in the body at 5 atmospheres of air pressure. As indicated previously, the tension of nitrogen in fatty tissues would, at equilibrium, be the same as in other tissues, but since nitrogen is about five times more soluble in fat than in blood, the total quantity of nitrogen contained by fatty regions would be relatively great. On decompression from 5 atmospheres of air pressure, nitrogen would be the chief constituent of bubbles because, while oxygen and carbon dioxide are present, the amount of nitrogen is proportionately a great deal larger. Even the theoretic tensions of oxygen and carbon dioxide in tissues are difficult to calculate because they are metabolic gases. However, by using the alveolar equation we can approximate the tensions of oxygen in alveolar air and, hence, in arterial blood.

Table I shows the theoretic tension of gases in the arterial blood at 5, 1, and 1/5 atmospheres.

TABLE I

*Theoretic tension of gases in arterial blood of the body*

| Pressure (mm. Hg) | $P_{H_2O}$ | $P_{CO_2}$ | $P_{O_2}$ | $P_{N_2}$ | Comment |
|---|---|---|---|---|---|
| 152 (1/5 atm.) | 47 | 38 | 65 | Trace | Breathing 100% oxygen |
| 760 (1 atm.) | 47 | 40 | 103 | 570 | Breathing air |
| 3,800 (5 atm.) | 47 | 40 | 741 | 2,972 | Breathing air |

According to the alveolar equation (using an RQ of 0.82) the tension of dissolved oxygen in the arterial blood at 5 atmospheres of air pressure would be about 741 mm. Hg. The $P_{CO_2}$ is given as 40 mm. Hg because increased respiration would reduce its value if there was a tendency for its tension to rise. The most important things to note are the relatively large $P_{N_2}$ of 2,972 mm. Hg as compared to 570 mm. Hg at sea level and the "trace" of nitrogen in arterial blood at an altitude equivalent to 152 mm. Hg. The latter $P_{N_2}$ would depend on the period of denitrogenation before reaching altitude. Although the values shown in the table are given for arterial blood gas tensions, they do indicate that the bubbles which are formed during decompressions from 5 atmospheres to 1 atmosphere would be composed largely of nitrogen, whereas those formed on decompression from 1 to 1/5 atmospheres would very likely, even in the tissues, be composed of *gases other than nitrogen when equilibrium was attained.* It should be noted that this does not negate our previous statement that the *initial* bubble formed at altitude could be composed mainly of nitrogen gas.

Let us assume that a gas nucleus was present and that a bubble was formed in the arterial blood stream on rapid decompression from 5 atmospheres of pressure to 1 atmosphere. If we use the

values given in table I, the theoretic composition of the bubble would be:

| | | |
|---|---|---|
| $H_2O$ vapor, mm. Hg | 47/3,800 | = 1.2% by volume |
| $CO_2$, mm. Hg | 40/3,800 | = 1.0% by volume |
| $O_2$, mm. Hg | 741/3,800 | = 19.5% by volume |
| $N_2$, mm. Hg | 2,972/3,800 | = 78.3% by volume |

The conclusion is that this gas bubble would be composed mainly of nitrogen when the decompression is made from 5 atmospheres to 1 atmosphere.

## GRADING OF SYMPTOMS

Before beginning a discussion of the individual symptoms which, collectively, constitute altitude dysbarism, we can grade these symptoms according to severity. Several different schemes of grading symptoms have been used. In our discussions we shall use a slight modification of the system adopted by Gray (103) and used to classify Randolph Field data.

*Grade 1.* Pain symptoms which disappear after a time at altitude or are intermittent, even though the individual does not descend to an altitude below that where they appeared.

*Grade 2.* Pain symptoms which persist as long as the individual remains at or above the altitude where they appeared, but which are not, themselves, severe enough to force descent.

*Grade 3.* Pain symptoms which are severe enough to force premature descent from the altitude at which they appeared, but which are not accompanied by secondary symptoms of the sort that would indicate the autonomic and circulatory systems had become involved.

*Grade 4.* Symptoms, such as pallor, sweating, faintness, dizziness, etc., which indicate that the autonomic and circulatory systems are displaying a reaction that might lead to collapse, regardless of the number or degree of painful symptoms which may also exist.

Some investigators have used the terminology of "tolerable symptoms" to indicate grades 1 and 2 as listed above, and the term "intolerable symptoms" to represent grades 3 and 4 which cause premature descent from altitude.

Obviously, the grading of symptoms allows us to quantitate data, but it should be remembered that we are attempting to quantitate symptoms which are subjective. By this, we mean that individuals differ within a rather wide range as to their ability or willingness to tolerate symptoms at altitude. Therefore, the "quantitative" data which is presented, especially in grades 2 and 3, will be especially susceptible to error because of the qualitative differences in an individual's symptom tolerance.

The acceptance, however, of this simple classification will allow us to better appreciate the overall incidence of symptoms at altitude when representative tables of such data are presented. There could be some disagreement in classifying only a very small group of individuals who had no bends, chokes, abdominal symptoms, etc., but who experienced vasomotor phenomena at the peak altitude or even on ascent. In many instances, these cannot be classified as symptoms of altitude dysbarism but are probably due to hypoxia as a result of poor mask fitting or apprehension, which result in hyperventilation. Both of the latter conditions, when they occur, usually cause descent from altitude, especially if vomiting or syncope is a part of the syndrome.

In the past, grading of symptoms due to altitude dysbarism has been confined to the more spectacular symptoms of bends, chokes, and central nervous system effects. Many investigators have failed to report the incidence of abdominal gas pains or have reported them as miscellaneous. The remaining symptoms of barotalgia, barosinusitis, etc., also have been treated as special conditions because, if included, they would tend to alter the incidence of symptoms markedly. All symptoms, however, may be incapacitating and from that viewpoint are important.

## SYMPTOMATOLOGY OF ALTITUDE DYSBARISM

### Bends

The first reference to bends as a symptom of dysbarism occurs in the literature on caisson disease (129, 133). Because there was an exacerbation of the pain when the individuals affected were in the erect position, they often assumed a stooping or "bends" position.

By definition, bends is a clinical manifestation of hypobarism consisting of pain referred to the joints, bones, or muscles.

**Location of pain of bends.** The pain associated with bends at altitude is variable in almost all except a few characteristics. The location of the pain is most often described as being deep in the joints, bones, or muscles of an extremity, including the hip and shoulder. For some unknown reason, instances of pain in such regions as the sternum, ribs, vertebrae, and cranium have been conspicuously absent but have been reported (111). Gray (102) pointed out that it may be significant that the bones of the extremities contain yellow bone marrow rather than red and are comparatively avascular with a high concentration of fat. Perhaps the deep pain "felt in the bone" is best explained by bubbles causing ischemia of bone or distortion of the periosteum. In any event, the synovial cavity can withstand considerable distention without pain and so it is thought that the pain does not arise from gaseous distention of joint cavities per se. Most often, even in an extremity, the pain is diffuse and *poorly localized*. According to School of Aviation Medicine data on 158 subjects at 38,000 feet, about 54% are recorded as joint pains, 26% as chiefly muscle, and 20% as being felt deep in the bone (109). In character, most of the pains are of a *deep*, boring or aching, dull, protopathic type sometimes resembling the dull pain of a tetanus antitoxin injection. Many individuals, after descent caused by a grade 3 uncomplicated bends pain at altitude, have a poor memory of the pain and wonder why they could not have tolerated it longer. In some instances, the localization is very definite and the individual will isolate a small area, especially in the finger or wrist in which the pain is

felt. When this discretely finite type of pain is described in an extremity, it is usually localized over a periosteal insertion of a tendon (patella, deltoid, etc.).

The onset of bends pain may be gradual or fulminating and vary in duration from single or intermittent twinges to one which is steady. No dogmatic statement can be made concerning the progression of bends pain at altitude. Evelyn (71) noted that at the onset, pains were usually mild, but in 11 of 175 cases they were acutely severe. Mild degrees of aching discomfort have developed slowly or rapidly to pains which were sharp and incapacitating. Conversely, moderately severe pains, which if they continued would become intolerable, have been known to spontaneously disappear for the remainder of the stay at altitude. In 3,744 ascents to altitude there were 1,253 instances of limb pain. Of these, 639 were mild, 521 moderate, and 93 severe. Of the mild pains, 33% disappeared, 29% were persistent, and 38% became of stronger intensity (230). One feature of moderate or severe joint pain is the tendency of the muscles to splint the joint, with weakness or loss of movement. It is usually a pseudoparesis or a pseudoparalysis, the muscles being tense at first, perhaps, but later flaccid. Obviously, function is impaired and if the arms and hands are affected, there may be a coarse tremor with loss of useful motion until descent is made. Acute or delayed true paresis or paralysis may occur which is of varying duration (see report on "Neurocirculatory Collapse at Altitude"). During or after descent all symptoms usually disappear. In some instances a feeling of weakness persists, and in a few cases soreness may be noted for several days. This may be due to extensive dissection of fascial planes by large bubble collections.

Lund and Lawrence (168) concluded that bends pain may be caused by collections of gas in the fascial and intermuscular septal planes. During exposure of human subjects to simulated altitudes of over 34,000 feet in a low pressure chamber, the subjects who developed severe bends in areas suitable for massage were lowered to and maintained at an altitude at which the bends pain was decreased or absent. A firm massaging action was instituted in 20 cases of bends. In 11 instances, pain was reinduced or increased

at the lower altitude. In four other instances, the shift of pain closer to the joint ahead of the massaging hand was noted. In one case of these latter four, a rolling tourniquet was accompanied by the movement of pain from a point just below the patella ahead of the tourniquet to the ankle. Release of the tourniquet was followed by return of pain to the original site at the knee.

If we assume that the "bubble" is the initiating cause, then the *importance of a bubble in initiating pain must be that of its location.* Intravascular bubbles, for example, could produce pain by causing ischemia. Extravascular bubbles may produce pain by (a) mechanical distortion of tissue and direct stimulation of pain receptors, (b) by a localized expansion which produces direct external pressure on blood vessels and ischemia, or (c) by initiating reflex vasoconstriction which produces ischemia. Perhaps several of the mechanisms are involved because large collections of gas have been visualized by x-ray with little or no pain recorded (43, 238) and, on the other hand, definite bends symptoms have been recorded in limbs when x-rays taken at altitude during the flight revealed no such collections of gas (43). Because of the latter condition, it was postulated that a small bubble in a "critical focus" could result in symptoms out of proportion with bubble size. Perhaps the pain mechanism in such instances is that of ischemia due to vasoconstriction rather than that of a small bubble in a critical focus. It appears quite likely that more than one mechanism may cause bends pain, and in any given subject the chief mechanism causing pain may be different from that in another individual.

There is general agreement that the greatest number of bends is located in the knees and the shoulders. Individual reports differ as to whether the knee or shoulder has the greater incidence (table II). The incidence of incapacitating bends, however, seems to be greater in the knees than in the shoulders (183). Most data indicate that the occurrence of bends is equally distributed to both sides of the body although Bierman et al. (32) found a slight predominance on the right side.

Why the knees and shoulders are especially affected by bends is not entirely clear. It is probably a combination of such factors

TABLE II

*Locaton of bends symptoms—percentages*

| Site | Ref. 109 | Ref 228 | Ref. 230 | Ref. 231 | Ref. 183 | Ref. 36 |
|---|---|---|---|---|---|---|
| Shoulder | 19.7 | 24.0 | 23.5 | 21.5 | 32.4 | 10.2 |
| Upper arm | 7.1 | — | 9.9 | — | 4.7 | 2.6 |
| Elbow | 10.0 | 12.0 | 7.5 | 5.2 | 10.3 | 3.8 |
| Forearm | 3.9 | — | 2.2 | — | — | 1.0 |
| Wrist | 9.9 | 8.0 | 11.4 | 11.2 | 16.5 | 1.6 |
| Hand and fingers | 7.2 | 15.0 | 6.1 | 2.0 | 3.9 | 1.6 |
| Total upper extremity | 57.8 | 59.0 | 60.6 | 39.9 | 67.8 | 20.8 |
| Hip | 3.0 | 3.0 | 1.9 | — | 1.9 | 2.6 |
| Thigh | 5.0 | — | 1.4 | — | — | 1.0 |
| Knee | 23.2 | 32.0 | 22.6 | 48.4 | 23.2 | 54.8 |
| Lower leg | 3.8 | — | 3.4 | — | — | 2.1 |
| Ankle | 5.0 | 10.0 | 7.4 | 7.7 | 3.6 | 11.3 |
| Foot and toes | 2.2 | 6.0 | 2.7 | — | 0.7 | 7.0 |
| Total lower extremity | 42.2 | 51.0 | 39.4 | 56.1 | 39.4 | 78.8 |

as circulation, fat deposits, development of mechanical tensions, etc. Swann and Rosenthal (231) theorized that, because of the position of the joints, rising bubbles might be trapped in these two areas. In an experimental study (247) concerned with air embolism, the theory was advanced that the buoyance of air determines its distribution in various parts of the body. Also, a fatal diving case has been reported (95) in which there were far more bubbles in the legs than in the brain since the individual was in the head-down position when the body was recovered. It was advised that such casualties should be carried in the head-down position to keep bubbles from the brain. According to this reasoning, elevation of an arm above the head should cause bends to occur in the wrists and fingers. This was found to be true (232), but the fact remains that the same maneuver affects the circulation also and, hence, bubbles may be only part of the mechanism.

**Incidence of bends.** Of those hypobaric disturbances which are thought to be caused by evolution of gas from solution resulting

in bubble formation, *bends* is the most frequent significant symptom (78, 103, 183, 231). There are a number of factors which affect the incidence of bends at altitude. Because of variations in experimental design and technic, many of the individual sets of data cannot be compared directly with each other. Fortunately, however, the principal laboratories have conducted several different experimental series, the results of which can be compared with their own control tests. On this basis, several important conclusions may be stated. In general, the factors which have been considered to possibly affect the incidence of bends at altitude may be placed into several categories:

*Physical factors*

1. Rate of ascent
2. Altitude attained
3. Duration of exposure
4. General environmental factors

*Physiologic factors*

1. Age
2. Obesity
3. Exercise
4. Previous injuries
5. Physical fitness
6. Hypoxia
7. Diet and fluid intake
8. Repeated exposure

*Miscellaneous factors*

1. Apprehension
2. Race and nationality

## Rate of ascent

Theoretically, the more rapidly an ascent to altitude is made, the greater should be the incidence of bends. That the rate of decompression is important to the incidence of bends has been known for a long time among personnel associated with caisson and diving operations. In accordance with the bubble theory, and assuming that nitrogen is the gas most important in initial formation of a bubble, the slower the rate of ascent to altitude the longer the time of denitrogenation. More rapid ascents would allow less time to establish equilibrium of gaseous diffusion between the body depots of nitrogen and the environment. Obviously, with rapid ascents it is also true that the circulatory system has less time to adjust.

Examination of available data on altitude dysbarism is disappointing in that it is not easy to show that rates of ascent make a decided difference in the incidence of symptoms, even though Armstrong (13) reported the appearance of bubbles in animals at lower altitudes when faster rates of ascent were used. Also, Catchpole and Gersh (52) showed a higher average bubble incidence in rabbits decompressed to 45,000 feet in 3 to 10 seconds as compared to a rate of 10 minutes. The percentage of deaths was also higher at the faster rate.

Armstrong (16) had theorized that a rate of ascent of 78 feet per minute or more would favor bubble formation. However, in an experiment lasting 16 hours with a mean decompression rate of 45 feet per minute, one individual still developed serious symptoms (184).

Evelyn (70-72) used average rates of ascent varying from 500 to 4,000 feet per minute. He concluded that variations in this range caused no difference in the incidence of bends. Gray (97) found that rates of ascent up to 4,000 feet per minute had no significant effect on the incidence of serious symptoms.

In contrast, Griffen et al. (111) obtained data to show that the susceptibility to bends was markedly increased by a rate of ascent of 5,000 feet as compared to 1,000 feet per minute. These authors concluded that the rate of ascent per se seemed to influence the incidence of bends regardless of the fact that the slower rate provided a longer period of denitrogenation.

It would seem logical to believe that the incidence of symptoms would be greatly increased in instances of explosive decompression. Actually, studies which exposed humans to altitude have not provided as clear-cut evidence as one would wish to see on this important subject. Hitchcock, quoted by Fulton (82), explosively decompressed humans from 20,000 to 40,000 feet and, although there was an increased incidence of bends and chokes from 55 to 65% as compared with the slow ascents, the differences were not thought to be significant. When the explosive decompression ranged from 10,000 to 38,000 feet, there was a significant increase from 62 to 88% as compared with the slow ascents. Explosive decompressions from 27,500 feet to 45,000 feet, using pressure breathing, resulted in only a 55.2% incidence as compared to 40.6 for the controls.

COMMENT. It is logical o believe, but difficult to prove from existing data, that a rapid rate of decompression to altitude increases the incidence of dysbarism. It has proved true in caisson or diving operations. It is quite possible that other factors are much more important in altitude dysbarism and have thus affected the accuracy of the data. It is fair to conclude that a very slow ascent, either continuous or in stages, would result in a lower incidence of dysbaric symptoms than a very rapid ascent. Very likely, ranges of ascent between 1,000 to 5,000 feet per minute would give no significant differences because of the greater effect of other variations.

## Altitude attained

There is little question that the higher the altitude attained the greater is the incidence of bends and other hypobaric phenomena. Obviously, the higher the altitude the larger the bubble size and, perhaps, the greater the number of bubbles. Also, Knisely (158) has noted that the extent of vasospasm was greater in the scleral vessels as the altitude was increased, and this correlated very well with the incidence of bends.

So many factors enter into this consideration that such conditions as rest, exercise, and rate of ascent must be mentioned when one speaks of a "bends altitude." From 20,000 to 25,000 feet has been considered as a critical range of altitude for the occurrence of aero-embolism in man (184). Houston (135) reported on 20 individuals who made 387 ascents to altitude up to 22,500 feet. Six of these experienced aero-embolism on approximately 15 occasions beginning as low as 17,000 feet. In 2 of 6 cases the pain was incapacitating. Symptoms may occur under 20,000 feet, but the incidences are small (217) and are usually associated with recent injury, etc. (6, 149). In this connection, Krisely (158) has noted vasoconstriction to begin in the scleral vessels at about 20,000 feet. Tables III and IV show the data which have been obtained. Although there is no perfect correlation between the number and grade of bends with the altitude, the trend can be very easily noted. Cook et al. (58) concluded that an increase in altitude from 30,000 to 38,000 feet increased the incidence and severity of dysbaric symptoms more than did doubling the frequency of exercise at either altitude. The introduction of exercise increases the incidence of descents as much as adding 5,000 feet to the altitude (103).

The small animal studies which have been done clearly indicate that the appearance and size of bubbles are also dependent on the altitude attained. However, the small animals are relatively refractory to bubble formation. Armstrong (13) reported the appearance of bubbles in the blood of animals at 35,000 feet. In bull frogs having muscular activity, no bubbles were seen below 60,000 feet. Violent exercise caused bubbles to appear as low as 20,000 feet (255). Various conditions, such as exercise, are necessary to produce bubbles in cats at 35,000 feet, in rabbits at 40,000 feet (2), and in rats at 50,000 feet (254).

Paradoxically, bends or chokes can occur on descent or be exacerbated by descent to a lower altitude (203). The relatively few cases in which it has occurred can be explained by assuming that at the peak altitude the bubbles were in a relatively insensitive area. On descent, the small bubble size allowed movement to a more sensitive area. In general, both the altitude attained and exercise are shown to be important factors.

## TABLE III

*Incidence of bends at various altitudes—no exercise*

| References | Altitude (ft.) | Duration of flight (hr.) | Rate of ascent (ft./min.) | No. of tests | Total bends symptoms | | Grades 1 and 2 | | Grades 3 and 4 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | No. | % | No. | % | No. | % |
| 216 | 26,000 | 0.33 | 3-5,000 | 65 | 1 | 1.5 | 1 | 1.5 | 0 | 0 |
| 216 | 28,000 | 0.33 | 3-5,000 | 80 | 1 | 1.3 | 1 | 1.3 | 0 | 0 |
| 216 | 30,000 | 0.33 | 3-5,000 | 92 | 4 | 4.3 | 4 | 4.3 | 0 | 0 |
| 96 | 33,000 | 2.0 | 3,000 | 100 | 18 | 18.0 | 13 | 13.0 | 5 | 5.0 |
| 230 | 35,000 | 2.0 | 1,167 | 3,744 | 1,253 | 33.0 | 573 | 15.3 | 680 | 18.7 |
| 211 | 35,000 | 3.0 | 1,000 | 584 | 131 | 13.1 | 56 | 5.6 | 75 | 7.5 |
| 183 | 38,000 | 1.0 | 2,000 | 7,664 | 2,100 | 27.4 | 866 | 11.3 | 1,234 | 16.1 |
| 100 | 38,000 | 2.0 | 4,000 | 239 | 75 | 31.3 | 39 | 16.3 | 36 | 15.0 |
| 211 | 38,000 | 3.0 | 1,407 | 4,228 | 780 | 18.4 | 574 | 13.5 | 206 | 4.9 |
| 83* | 38,000 | 3.0 | — | 4,524 | — | — | — | — | 649 | 14.3 |
| 83 | 38,000 | 3.0 | — | 378 | — | — | — | — | 69 | 18.3 |
| 141 | 40,000 | 1.0 | 5,000 | 105 | 56 | 53.0 | 23 | 21.9 | 33 | 31.4 |
| 142† | 47,500 | 1.0 | 5,000 | 50 | 22 | 44.0 | 11 | 22.0 | 11 | 22.0 |

*Continuous flow $O_2$; no $O_2$ up to 18,000 feet. Stop at 28,000 feet for indoctrination.

†Intermittent pressure breathing.

## TABLE IV

*Incidence of bends at various altitudes—with exercise*

| References | Altitude (ft.) | Duration of flight (hr.) | Rate of ascent | No. of tests | Total bends symptoms | | Grades 1 and 2 | | Grades 3 and 4 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | No. | % | No. | % | No. | % |
| 135 | 17-20,000 | 0.25 | 4,000 | 387 | 15 | 3.9 | 13 | 3.3 | 2 | 0.6 |
| 96 | 23,000 | 1.0 | 3,000 | 117 | 9 | 7.7 | 8 | 6.8 | 1 | 0.9 |
| 96 | 23,000 | 2.0 | 3,000 | 195 | 25 | 12.8 | 25 | 12.8 | 0 | 0 |
| 96 | 25,000 | 2.0 | 3,000 | 128 | 15 | 11.8 | 13 | 10.2 | 2 | 1.6 |
| 216 | 26,000 | 0.33 | 3-5,000 | 71 | 13 | 18.3 | 12 | 16.9 | 1 | 1.1 |
| 96 | 27,000 | 2.0 | 3,000 | 93 | 8 | 8.6 | 7 | 7.5 | 1 | 1.1 |
| 216 | 28,000 | 0.33 | 3-5,000 | 65 | 16 | 24.6 | 8 | 12.3 | 8 | 12.3 |
| 216 | 30,000 | 0.33 | 3-5,000 | 122 | 36 | 29.5 | 22 | 18.0 | 14 | 11.5 |
| 32 | 35,000 | 1.0 | — | 1,000 | 244 | 24.4 | 172 | 17.2 | 72 | 7.2 |
| 36 | 38,000 | 1.5 | 3,170 | 167 | 104 | 62.3 | 46 | 44.2 | 58 | 55.8 |
| 83 | 38,000 | 1.0 | — | 1,982 | — | — | — | — | 251 | 12.7 |
| 83 | 38,000 | 0.25 | — | 29,353 | — | — | — | — | 710 | 2.42 |
| 38 | 38,000 | 1.5 | — | 225 | — | — | — | — | 88 | 39.1 |

## Duration of exposure

The longer the time of exposure to a given altitude, the greater the number of individuals who will be affected by symptoms of dysbarism. This means that 40,000 feet for 15 minutes will, *in general*, not be as severe an exposure as 40,000 feet for an hour. This does not mean that an exposure of 15 minutes is without hazard, since symptoms may appear before 40,000 feet is attained and extremely severe symptoms can occur in less than 15 minutes at 40,000 feet.

Table V shows the incidence of symptoms in 30-minute periods at various altitudes. Although the data are restricted to exposures of 120 minutes, the total incidence increases. However, it has been noted that the longer an individual has been at altitude without developing symptoms, the less likely is he to develop symptoms as time goes on. This is probably explained by the fact that when breathing 100% oxygen he continues to denitrogenate as the exposure progresses.

## General environmental factors

Temperature. Swann and Rosenthal (231) were unable to correlate the incidence of bends with ambient chamber temperatures between 70° and 87° F. A similar lack of definite correlation was found in the temperature ranges of 75° to 94° F. (183).

In studies specifically designed to cover wider ranges of temperature, an effect on bends and chokes has been reported. Of 121 subjects seated at 38,000 feet with a chamber temperature of 100° F., 35.5% developed severe bends, whereas 47.3% of 112 subjects developed severe bends at a temperature of 55° F. (11). It was thought that possibly the skin and immediately adjacent tissues contain appreciable nitrogen and that the growth of bubbles in such cooled regions would be slower because of increased solubility, slower diffusion, and a decreased partial pressure of gas. This would delay the appearance of symptoms, but more symptoms would ultimately appear because of the decreased rate of nitrogen elimination. In the same tests there was a 10% incidence of chokes in the warm flights and a 16% incidence in the

## TABLE V

*Increase in incidence of symptoms with increase in time at altitude*

| Reference | No. of subjects with symptoms | Altitude | Time in minutes | | | | | | | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 0-30 | | 31-60 | | 61-90 | | 91-120 | | |
| | | | No. | % | No. | % | No. | % | No. | % | |
| 183 | 750 | 30,000 | 214 | 28.5 | 536 | 71.5 | — | — | — | — | Grade 3 and 4 bends |
| 230 | 1,328 | 35,000 | 560 | 32.1 | 382 | 28.8 | 267 | 20.1 | 114 | 8.6 | Total symptoms |
| 239 | 75 | 35,000 | 13 | 18.0 | 19 | 25.0 | 17 | 23.0 | 13 | 18.0 | Grade 3 and 4 bends |
| 109 | 194 | 38,000 | 30 | 15.5 | 80 | 41.2 | 49 | 25.3 | 20 | 10.3 | Grade 3 and 4 bends |
| 231 | 158 | 38,000 | 11 | 7.0 | 34 | 21.0 | 52 | 33.0 | 26 | 17.0 | Grade 3 and 4 bends |

cold. The difference was considered suggestive but not statistically significant. A second group of workers (112) found that subjects kept comfortably warm suffered significantly less from bends than the same subjects when underdressed in the cold. It was emphasized that the skin temperatures had to be kept at levels as high as those characteristic of warm environments and, hence, peripheral vasodilation was thought to be an essential factor. Fraser and Rose, quoted in a review of Canadian investigations (79), studied individuals exposed to 35,000 feet at temperatures of −10° and 70° F. The incidence of symptoms was greater at the lower temperature, the number of incapacitating bends being about double; on the other hand, the number of milder symptoms was only slightly increased. The same review quoted studies by Waters, who found that in a group of subjects at 35,000 feet and room temperature, or 30,000 to 32,500 feet at −10° F., the same subjects developing symptoms requiring descent from the cold chamber at the lower altitudes also developed such symptoms at room temperature while at 35,000 feet. These observations may be significant in indicating the importance of the circulation in the etiology of bends. It is also possibly of some significance that the incidence of incapacitating bends was somewhat higher in individuals with a low body temperature (oral) as compared with those with slightly increased temperatures (231).

Daily variations in barometric pressure. Among other analyses, it seemed desirable to correlate the incidence of dysbarism symptoms with the daily variation in barometric pressure. It is possible, for instance, that the pain of bends may be akin to arthritic malaise, and clinically, it is a common observation that the latter type of pain is exacerbated by changes in barometric pressure. It is of interest in this connection that Jones and Schiller (149) exposed 5 young adults with symptomatic arthritis or fibrositis to 3,000, 6,000, and 9,000 feet in a low pressure chamber. In 144 twenty-minute experiments they found a good correlation between altitude exposure and the incidence of pain in joints that had been asymptomatic at sea level.

In several studies in which the range of daily environmental pressure change was only about 10 to 20 mm. Hg, there was no

correlation with symptoms (42, 229, 231, 240). There was some question concerning the relationship of the relative humidity to symptoms of dysbarism. It was concluded, however, that the finding was not constant enough to be real (240).

Time of day and season. For some unknown reason it may be a fact that the incidence of "decompression sickness" (symptoms due to evolved gases such as bends, chokes, etc.) is higher in low pressure chamber runs conducted in the morning than in runs conducted in the afternoon. Thompson et al. (240) have reported that of 2,076 men given low pressure chamber flights to 35,000 feet during the hours of 0900 to 1200, 41% manifested decompression sickness; among 1,558 men during the hours of 1300 to 1600, only 29%; among 91 men during the hours of 1700 to 2000, only 22%. When the data were tabulated to pick out those 291 subjects who had three chamber runs in the morning and those 240 subjects who had all three chamber runs in the afternoon, there was a 39% incidence in the morning and only a 21% incidence in the afternoon. Further, there were 459 individuals who had both morning and afternoon chamber ascents. There was a 38.6% incidence in the morning as compared to 27.4% in the afternoon. The data obtained by Savely (211) indicate that descents occurred in 14% in morning flights, 9% in afternoon, and 12.5% in evening flights to 35,000 feet. Stewart et al. (228) showed that in 52.8% of 441-man runs, there were symptoms in the morning, whereas 32.8% of 399 subjects showed symptoms in the afternoon. The same type of results was obtained by Smith and collaborators (220). The data of Motley et al. (183) show the percentage incidence of bends on chamber ascents during various times of the day.

If the incidence of symptoms is greater in morning flights than in afternoon flights, it may be due to the fact that metabolism in general is lower during the morning, or more likely because of the various factors which cause metabolism to be lower—that is, the rate of gas exchange and altered circulation (124). It is pertinent to examine some of the possible relationships (table VI).

The data of Swann and Rosenthal (231) are in agreement (table VII).

Guest (114) reported data which agree with the other authors in that the greatest incidence of bends was in the morning flights. However, the evening incidence is contrary to the data of Motley et al. (table VIII).

## TABLE VI

*Incidence of bends and time of day (153)*

| Time | No. of subjects | Total bends | Grades 1 and 2 | Grades 3 and 4 |
|---|---|---|---|---|
| 0600 - 1000 | 8,468 | 17.9 | 12.2 | 5.7 |
| 0900 - 1300 | 9,986 | 16.6 | 11.0 | 5.6 |
| 1300 - 1700 | 10,109 | 15.5 | 10.8 | 4.7 |
| 1600 - 2400 | 8,301 | 15.5 | 10.8 | [illegible] |
| 1930 - 2230 | 7,317 | 11.6 | 7.3 | 4.3 |

## TABLE VII

*Incidences of bends and time of day (231)*

| | Morning | Afternoon |
|---|---|---|
| No. of man-flights | 2,060 | 1,842 |
| Grades 1 and 2 (%) | 13.4 | 9.7 |
| Grades 3 and 4 (%) | 4.9 | 3.9 |

## TABLE VIII

*Incidences of bends and time of day (183)*

| Time | No. of subjects | Percent incidence of bends |
|---|---|---|
| 0700 - 1200 | 2,693 | 30.0 |
| 1300 - 1800 | 2,593 | 15.4 |
| 1800 - 2300 | 1,341 | 20.7 |
| 2200 - 0400 | 210 | 11.9 |

All flights were at 38,000 feet for 3 hours.

Revici and co-workers (197) have conducted some preliminary clinical studies on the nature of pain associated with various chronic pathologic conditions. Variations in pain intensity in some clinical conditions appear to be associated with a general factor that is influenced by the time of day and by the intake of food. In this connection, changes in the blood pH have been shown to vary with the time of day (59). There was a possibility, therefore, that an actual relationship existed between variation in acid-base balance of the body and pain intensity. From their studies, Revici et al. have concluded that there are two distinct patterns of pain correlation. In *alkaline pain* the pain is of greater intensity when the body is relatively more alkaline and less severe when the body is more acid, and in *acid pain* the pain is more marked when the body is more acid and less painful when it is more alkaline. At the local pathologic site some abnormal metabolic activity leads to an accumulation of abnormal metabolites which alter the local pH. This local site may be alkaline or acid and, hence, the general acid-base balance changes may augment or limit the local pH deviation and influence the severity of the pain. The tests conducted on various types of patients apparently supported the above concepts, since strong alkalinizing agents administered orally may increase the severity of alkaline pain and relieve acid pain; and strong acidizing agents may act conversely. These concepts require a considerable amount of further experimental investigation, but it is of interest to speculate on the relationship of acid-base balance to the pain of bends.

Hodes and Larrabee (132) tested a small number of subjects repeatedly in a low pressure chamber at 38,000 feet for 2 hours using a moderate exercise. The susceptibility of several of these subjects to bends varied in a cyclic manner. This suggested that perhaps the susceptibility was influenced by physiologic factors which varied in a parallel manner. The physiologic factor considered was that of individual acid-base balance, since this factor is known to fluctuate during the day and from day to day in the same individual.

The acid-base balance could theoretically affect the incidence of bends in a number of different ways. It affects respiration;

the changes of carbon dioxide tension in tissues could affect the rate of bubble growth; changes in carbon dioxide tension may result in alterations of the peripheral circulation any may, hence, modify the denitrogenation of tissues as well as the local pH; and an acid-base change in local regions may alter the irritability of peripheral nerve. Hodes and Larrabee (132) pointed out that several studies of caisson disease contain data or indirectly support the concept that the incidence of dysbarism may be affected by the amount of expired carbon dioxide which accumulates in poorly ventilated diving helmets or tunnels. In their own tests, the alveolar $P_{CO_2}$ of experimental subjects was determined previous to ascent to 38,000 feet. When the results were grouped according to the alveolar $P_{CO_2}$ values before ascent, a correlation was found in that the incidence of severe bends decreased with decreasing $P_{CO_2}$. When the $P_{CO_2}$ was 43 to 45.5 mm. Hg in 7 cases, the bends was incapacitating; in the range of 40.9 to 42.9 mm. Hg on 30 tests, there were 60% forced descents; in the range of 38.0 to 40.8 mm. Hg on 31 tests, there were 55% forced descents; and, finally, all 5 tests were passed when the $P_{CO_2}$ was 35.1 to 37.9 mm. Hg. Ammonium chloride given to the subjects to produce a metabolic acidosis and reduce the $P_{CO_2}$ by hyperventilation was also thought to give a degree of protection from bends in some subjects, but not all. Several subjects had a particular anatomic site in which bends occurred regardless of the $P_{CO_2}$ level. It was concluded that other factors besides the acid-base balance were operative in susceptibility to bends.

The above studies show that acid-base balance may be an important factor in the mechanism of bends. The small number of subjects studied, and the tremendous number of other factors involved in bends, leave the results open to question. We can, however, mention a number of experiments and impressions which correlate fairly well with the concept that the acid-base balance is important. In one series of tests (44), 50 subjects were deliberately hyperventilated to the point of tingling and numbness or carpopedal spasm while seated at 40,000 feet. This would cause a respiratory alkalosis with a reduced alveolar $P_{CO_2}$ superimposed on the expected alkalosis due to the hypoxia at that altitude. In a control series of tests, the same subjects were exposed to

40,000 feet, but did not hyperventilate. Deliberate hyperventilation reduced the total symptoms of bends and chokes from 56 to 44% and reduced the intolerable bends and chokes from 20 to 8%. To remove the hypoxia factor, the same investigators also used 4 inches of intermittent positive-pressure breathing at 40,000 feet in 50 different subjects. By adjusting the pressure breather so that these subjects were hyperventilated to the point of tingling and carpopedal spasm, only 6% of the subjects developed intolerable bends and none developed chokes. Only 38% developed any symptoms of bends. It was suggested that hyperventilation caused a reduction in the body gases important to bubble growth. It is also of interest that the subjects noted a decrease in pain intensity on temporarily increasing the degree of hyperventilation. The latter observation may be of some importance and will be discussed in relationship to a few further concepts.

In experiments cited above (132) a high $P_{CO_2}$ was correlated with a high incidence of severe bends. Behnke (26) stated that empirical evidence points to a higher incidence of "bends" in association with a rise in the carbon dioxide level. Deliberate hyperventilation reduced the incidence of bends at 40,000 feet (44), and the subjects noted a decrease in pain intensity on temporarily increasing the degree of hyperventilation.

The question arises as to whether an increased $P_{CO_2}$ facilitates the growth of bubbles and, hence, increases bends, or whether an increased $P_{CO_2}$ contributes to body acidity and, hence, aggravates the local bends pain by augmenting local acidity. This would classify the pain of bends as an "acid pain." However, the concept of bends as an "acid pain" does not explain why the pain disappears so quickly on descent and reappears on ascent unless the "pain substance" or the pathologic metabolites are so labile that when the local pathologic situation is improved, then immediately the metabolites are no longer produced.

In most cases of bends, there is a complete reversal of symptoms on descent, even on rapid descent. It would be easier to explain this phenomenon on the basis of reduction of bubble size rather

than disappearance of local metabolites. It is true that in some instances residual soreness of local areas may persist after descent, but it may well be that the extensive tissue distortion by collections of gas with dissection of fascial planes in these particular cases is not a pathologic event that can be expected to be completely reversible in a few minutes or hours. Nims, quoted by Fulton (82), has developed a physical theory of bends pain which is based on the fact that gaseous bubbles growing in tissues must deform adjacent structures. According to this theory, the pain of bends is due to extravascular bubbles growing in "tight tissues." If the deformation pressure (D) exceeds a threshold value (D*), then nerve fibers are stimulated by the mechanical deformation of the tissues. The intensity of the stimulus is proportional to the excess of D above D* and depends on the type of tissue being deformed. The periosteum is very sensitive; ligaments, fibrous capsules of joints, tendons, fascia, and muscle would have different thresholds of sensibility. Obviously, the extent of deformation of tissues which persists at ground level will determine the duration that symptoms can be expected to persist.

There may be *seasonal variation* in the incidence of bends, but the data are confusing. It would seem that from the following observations there are unknown factors which influence susceptibility to bends or the methods of tabulating data have ignored known factors. (See tables IX and X.)

## TABLE IX

*Seasonal variation in the incidence of bends (239, 240)*

| Date | Morning runs | Percent decom. sickness | Afternoon runs | Percent decom. sickness |
|---|---|---|---|---|
| June 1942 | 1,856 | 37.8 | 669 | 33.3 |
| Aug. 1942 | 828 | 45.1 | 572 | 37.8 |
| Sept. 1942 | 2,076 | 41.0 | 1,558 | 29.0 |
| Mar. and Apr. 1943 | 6,932 | 32.3 | 4,312 | 24.7 |

TABLE X

*Seasonal variation in the incidence of bends (183)*

| Month | No. of subjects | Total bends (%) | Grades 1 and 2 (%) | Grades 3 and 4 (%) |
|---|---|---|---|---|
| Aug. 1943 | 6,352 | 19.0 | 12.9 | 6.1 |
| Sept. 1943 | 7,445 | 15.9 | 10.6 | 5.3 |
| Oct. 1943 | 6,981 | 13.5 | 9.1 | 4.4 |
| Nov. 1943 | 5,384 | 9.1 | 5.3 | 3.8 |
| Dec. 1943 | 3,277 | 10.7 | 7.1 | 3.6 |
| Jan. 1944 | 2,469 | 11.3 | 7.9 | 3.4 |
| Feb. 1944 | 3,493 | 12.5 | 8.5 | 4.0 |
| Mar. 1944 | 4,259 | 12.5 | 7.3 | 5.2 |
| Apr. 1944 | 4,425 | 11.8 | 8.3 | 3.5 |
| May 1944 | 420 | 12.4 | 8.1 | 4.3 |
| June 1944 | 684 | 9.2 | 5.7 | 3.5 |
| July 1944 | 1,020 | 14.0 | 6.8 | 7.2 |
| Aug. 1944 | 474 | 5.9 | 3.6 | 2.3 |
| Total | 46,683 | 8.8 | 4.6 | 13.4 |

*Physiologic Factors*

## Age

It was well known to caisson workers and divers that the older individual was more susceptible to decompression sickness. This was especially deplorable since they were the most experienced workers. Age per se is probably an important factor, but one must keep in mind the probability that with an increase in age there is an increase in mean body weight. The latter factor must be considered. In fact, it is probably true that the entire physical profile of age, weight, and height is more important than is a single criterion in determining susceptibility to dysbarism. It is not too surprising that age should be a factor in dysbarism, since the circulation certainly is altered with advance in years. The surprising fact is that these differences show up in a relatively narrow range of ages. Even in a small series, Thompson et al. (239) found that the incidence of symptoms was 12% in subjects 18 to 20 years of age, 22% in those of 21 to 23, 32% in those of 24 to 26, and 39% in those of 27 to 29 years. Table XI presents several similar sets of data.

## TABLE XI

*Age and susceptibility to dysbarism*

| Reference | Age | No. of subjects | % severe symptoms | % susceptible | % grades 1 and 2 bends | % grades 3 and 4 bends | Total bends |
|---|---|---|---|---|---|---|---|
| 184 | 19-25 | 119 | 13.4 | — | — | — | — |
| | 25-30 | 178 | 18.0 | — | — | — | — |
| | 30-35 | 65 | 24.5 | — | — | — | — |
| | 35-40 | 30 | 16.8 | — | — | — | — |
| | 40-45 | 8 | 37.5 | — | — | — | — |
| | 45-50 | 5 | 20.0 | — | — | — | — |
| 231 | 18-19 | 65 | — | 50.0 | — | — | — |
| | 20-21 | 204 | — | 55.3 | — | — | — |
| | 22-23 | 187 | — | 57.7 | — | — | — |
| | 24-25 | 123 | — | 61.2 | — | — | — |
| | 26-27 | 75 | — | 58.1 | — | — | — |
| | 28-29 | 60 | — | 62.5 | — | — | — |
| | 30-31 | 35 | — | 74.5 | — | — | — |
| | 32-33 | 28 | — | 70.0 | — | — | — |
| | 34-35 | 11 | — | 100.0 | — | — | — |
| 231 | 18 | 123 | — | — | 13.0 | 0.8 | 13.8 |
| | 19 | 528 | — | — | 11.9 | 4.2 | 16.1 |
| | 20 | 615 | — | — | 10.7 | 3.6 | 14.3 |
| | 21 | 516 | — | — | 9.3 | 3.7 | 13.0 |
| | 22 | 453 | — | — | 10.4 | 6.0 | 16.4 |
| | 23 | 246 | — | — | 11.4 | 9.0 | 20.4 |
| | 24 | 200 | — | — | 13.0 | 7.0 | 20.0 |
| | 25 | 144 | — | — | 13.9 | 7.0 | 20.9 |
| | 26 | 125 | — | — | 9.5 | 7.1 | 16.6 |
| | 27 | 123 | — | — | 14.6 | 6.5 | 21.1 |
| | 28 | 94 | — | — | 16.0 | 5.3 | 21.3 |

TABLE XI (Continued)

| Reference | Age | No. of subjects | % severe symptoms | % susceptible | % grades 1 and 2 bends | % grades 3 and 4 bends | Total bends |
|---|---|---|---|---|---|---|---|
| 183 | 18 | 2,356 | — | — | 6.9 | 2.5 | 9.4 |
| | 19 | 9,363 | — | — | 8.5 | 3.5 | 12.0 |
| | 20 | 8,250 | — | — | 9.8 | 4.0 | 13.8 |
| | 21 | 7,222 | — | — | 8.6 | 3.9 | 12.5 |
| | 22 | 4,736 | — | — | 9.4 | 4.9 | 14.3 |
| | 23 | 3,580 | — | — | 8.1 | 4.9 | 13.0 |
| | 24 | 2,356 | — | — | 8.7 | 5.6 | 14.3 |
| | 25 | 2,229 | — | — | 10.1 | 5.8 | 15.9 |
| | 26 | 2,081 | — | — | 9.4 | 5.1 | 14.5 |
| | 27 | 1,571 | — | — | 10.6 | 4.7 | 15.3 |
| | 28 | 155 | — | — | 7.1 | 5.7 | 12.8 |
| | 29 | 59 | — | — | 10.0 | 3.4 | 13.4 |
| | 30 | 74 | — | — | 3.1 | 2.1 | 5.2 |
| | Over 30 | 141 | — | — | 11.8 | 8.3 | 20.1 |

## Obesity

Long considered an important factor in caisson disease in divers, obesity has been shown to be a factor in altitude dysbarism (79, 183, 231, 240). The data of Motley et al. (183) on 44,181 trainees show that weight is a factor in the frequency and severity of bends (table XII). If the incidence of bends were taken for all of the subjects below 160 pounds, it would be 8.5% as compared to 10.7% for those above that weight. Various tabulations of weight-height (linear density), surface area, and ponderal indices show that the larger, heavier individuals are more susceptible to dysbarism. Behnke and co-workers (21, 27, 28) have expressed the concept of body density as an index of obesity. Rathbun and Pace (185, 193) have stated relationships for specific gravity as have Behnke et al. (27). Savely (211) somatotyped 184 of 187 men who were exposed to altitude. The degree of ectomorphy (tendency to linearity and slimness of physique) was found to be significantly higher in 98 men who did not develop symptoms than in those with symptoms.

### TABLE XII

*Bends and weight (modified from ref. 183)*

| Weight (lb.) | No. of subjects | Percentage of bends | | |
|---|---|---|---|---|
| | | Grades 1 and 2 | Grades 3 and 4 | Total |
| 130 | 912 | 4.8 | 2.2 | 7.0 |
| 130-134 | 1,237 | 6.0 | 2.1 | 8.1 |
| 135-139 | 1,824 | 7.4 | 2.0 | 9.4 |
| 140-144 | 3,346 | 6.8 | 2.7 | 9.5 |
| 145-149 | 5,045 | 5.1 | 2.1 | 7.2 |
| 150-154 | 6,631 | 6.8 | 2.5 | 9.3 |
| 155-159 | 6,719 | 5.7 | 2.4 | 8.1 |
| 160-164 | 5,657 | 6.9 | 2.9 | 9.8 |
| 165-169 | 4,208 | 7.4 | 2.8 | 10.2 |
| 170-174 | 3,596 | 7.2 | 3.8 | 11.0 |
| 175-179 | 2,060 | 7.3 | 3.8 | 11.1 |
| 180-184 | 1,723 | 8.0 | 3.9 | 11.9 |
| 185-189 | 1,136 | 8.4 | 3.5 | 11.9 |
| 190-194 | 600 | 7.3 | 3.8 | 11.1 |
| 195-199 | 337 | 8.0 | 5.6 | 13.6 |
| 200 | 150 | 5.3 | 5.3 | 10.6 |

The correlation between obesity or age and susceptibility is such as to allow prediction regarding the behavior of weight or age groups but not of individuals. As Gray (103) has stated, "These predictions resemble life insurance statistics which accurately predict the death rate but do not disclose which individuals are to die." The individual exceptions to the generalizations that old or fat people get bends are sometimes very glaring.

## Exercise

Exercise is one of the most important factors influencing bends and chokes at altitude. Deep knee bends, pushing, and other strains at altitude have been used to show that exercise increases the incidence of bends and descents as much as adding 3,000 to 5,000 feet to the altitude of the exposure (71, 74, 75, 99, 220, 252). The data obtained by Gray (99) and table XIII show that the performance of exercise at altitude lowered the threshold for the occurrence of symptoms from 32,000 feet to 27,000 feet and increased the relative importance of bends as a cause of descent (tables III and IV). Although exercise tends to promote symptoms in all parts of the body, the region most often affected is the part which is exercised. The incidence of bends and chokes in subjects who are seated is less than that of subjects who perform a mild exercise at altitude (220). In general, a severe exercise causes an increase in the incidence and severity of bends and chokes. Even isolated exercise of the hands and wrists as by a two-hand dynamometer resulted in a 75% incidence of bends as

TABLE XIII

*Effect of exercise on bends (99)*

| Altitude | Man-flights | Total descents (%) | Comment |
|---|---|---|---|
| 33,000 | 100 | 6.0 | No exercise |
| 33,000 | 143 | 24.5 | With exercise |
| 35,000 | 429 | 16.1 | No exercise |
| 35,000 | 149 | 43.6 | With exercise |
| 38,000 | 223 | 33.1 | No exercise |
| 38,000 | 56 | 58.9 | With exercise |

compared with a spontaneous incidence of 7% (11). Relief of bends produced in this manner by local compression related the cause to bubbles rather than ischemia.

Exercise increases the formation of bubbles in animals exposed to altitude (115, 119, 122). Conversely, bubble formation is decreased in anesthetized animals exposed to the same altitude, presumably because muscle tensions are decreased (115). In addition, the local formation of carbon dioxide gas during exercise contributes to the factor (t) in the equation $\Delta P = t - P$.

## Previous injuries

There may be a correlation between the occurrence of bends referred to a joint and the history of that particular joint being the site of a previous injury. Houston et al. (137) studied 1,538 man-ascents to altitude and determined the coincidence of bends at the site of previous injuries to be 7.2%, which was thought to be significant. Thompson et al. (240) and Gray (103) questioned whether the site of old injuries is associated with a greater incidence of bends although recent injuries may be a predisposing factor. Allan (6) cited several instances of recent injuries, one of which was the case of a combat pilot who developed an incapacitating pain in the left elbow at 12,000 feet. Three weeks later the symptoms occurred at 10,000 feet and were severe enough to cause descent. Examination by x-ray revealed traumatic calcification overlying the internal and external condyles of the left humerus. Further test exposures in the low pressure chamber caused the appearance of typical bends in the left elbow at 12,000 feet. Jones and Schiller (149), referred to previously, tested 5 young adults exhibiting symptomatic arthritis or fibrositis (without demonstrable joint or tissue pathology) at various altitudes. A definite correlation was found between exposure to altitude and the incidence of pain in joints that had been asymptomatic at sea level. The occurrence of joint pains at these low altitudes again suggests that such factors as hypoxia, causing circulatory impairment and alterations in cellular metabolism, etc., are concerned in the production of "typical" bends pain—that is, in addition to "bubbles" which could be formed at lower altitudes in injured tissue.

Thompson et al. (240) could not relate old injuries to the incidence of bends, but subjects given a blow on the superior and anteromedial aspect of the tibia experienced an increased incidence of bends in this region on subsequent exposure to 35,000 feet.

## Physical fitness

It seems reasonable to suppose that physical fitness could be an important factor in determining susceptibility to dysbarism. It is probably true that a seriously unfit group would not perform as well at altitude as a group in good physical condition. However, no relation between the state of physical fitness and the incidence of bends was found in a group of cadets (154). Of 197 subjects, 167 who completed a 3-hour classification test at 38,000 feet had an average score of 49.20 on the AAF Physical Fitness Test, whereas 30 subjects who failed this classification flight had a rating of 47.63. The lack of differentiation between the two groups may have been due to the severity of the test at altitude, the lack of adequate criteria for physical fitness, or both. The one study cited emphasized the need for more precise data and criteria.

## Hypoxia

Individuals exposed to brief periods of hypoxia before attaining a peak altitude had the same overall incidence of bends as did subjects given oxygen continuously (183). It may be significant that the hypoxia subjects had a decreased incidence of incapacitating bends as compared to the other groups. Smith (218) also determined that hypoxia at altitude did not increase the incidence of decompression sickness since a smaller number of symptoms occurred during these tests as compared with others. He did not consider the decrease significant. In connection with what has been discussed previously, it would seem possible that hyperventilation resulting from hypoxia reduces tissue carbon dioxide and, thus, reduces the tension of a gas which facilitates bubble growth. This view receives some support from the observation that deliberate hyperventilation by subjects seated at 40,000 feet decreased the incidence of intolerable bends and chokes from a

control value of 20% to 8%. It is also possible that hypoxia promotes an increase in blood flow through tissues and, thus, affects bubble formation. At the present time we must conclude that if hypoxia is a factor, its effects are masked by other factors.

## Diet and fluid intake

It was concluded that the incidence of bends symptoms was not related to the taking of food within the previous 12 hours (228), although fluid intake appeared to be significant. Seven subjects were repeatedly exposed to 38,000 feet with a mild exercise while on control, high protein, high carbohydrate, and high fat diets (42). The high protein diet significantly increased and the high carbohydrate diet significantly decreased the incidence of incapacitating bends. The high protein diet hastened the time of bends onset and decreased the average time subjects were able to stay at altitude. The high carbohydrate diet delayed the time of bends onset and increased the average time at altitude. The high fat diet had no significant effect on bends. Since these effects were observed with extremes in diet, it is unlikely that ordinary diet conditions have an appreciable influence on susceptibility to bends.

Individuals of high average daily fluid intake were, in general, less susceptible to symptoms than those of low intake (228), which agreed with the previous findings of Warwick (249, 250). Restriction of fluid intake for a 2-week period in a group of 6 men resulted in a general increase in susceptibility to dysbarism. The ingestion of large amounts of distilled water decreased the tolerance of 4 out of 6 subjects, whereas the ingestion of moderately large amounts of isotonic saline resulted in a general increase in tolerance. It was concluded that the relationship seemed definite, but was not simple, because the possibility existed that whatever controls an individual's desire for water may be more closely linked with susceptibility than the water itself. It seemed easier to predict susceptibility by knowing a person's propensity to drink water than it was to alter his susceptibility by altering his fluid intake (228).

## Repeated exposure

The question has often arisen as to whether repeated exposures to high altitude increases or decreases an individual's tolerance. Of 19 low pressure chamber technicians who were exposed to 30,000 feet from 76 to 288 times, 13 (68%) became less resistant to bends (41). This occurred when exposures were as frequent as one and sometimes two a day. Later, it was shown that rest periods of several days or more seemed to have a beneficial effect in preserving tolerance to bends. Houston (136) mentioned a medical officer, age 33, who had made about 300 ascents to altitude in 4 years with "increasing susceptibility to bends." Another study (215) indicated that certain individuals in the resistant and intermediate categories could develop a progressive loss of resistance with repeated exposures to 35,000 feet or above. In a later report (217), the same group questioned the concept of increasing susceptibility of individuals on repeated exposure to 20,000 feet.

Only 1 of 7 individuals exposed repeatedly to 38,000 feet appeared to become more susceptible with time (42), and Stewart et al. (228) speak of an "acclimatization effect" to dysbarism which reduced the total incidence of symptoms over a period of 14 consecutive daily runs. The effect was not noted in susceptible subjects. Several small groups of subjects were exposed to altitude up to 40,000 feet repeatedly but showed no symptoms of fatigue, and their blood sugar curves were normal (184).

A single exposure to high altitude often causes a tension-type fatigue. This is especially true if symptoms were experienced. During the course of many studies, there have been several opportunities to observe the possible effects of prolonged and frequent exposure. The Canadian studies summarized by Fraser et al. (79) have failed to demonstrate any persistent or progressive ill effects of general importance. Evelyn (70-72) studied 40 men for 8 weeks. The respiratory and renal systems were examined before and after, as was the blood picture. The only possible change was in the blood cholesterol, but even here, there was some question. In the group of 40, the average cholesterol value increased from 193 to 214; and in the 10 men with the longest

exposure, it increased from 186 to 212. In 4 men who had the most severe symptoms, it increased from 215 to 258. The relationship between blood cholesterol and susceptibility to dysbarism may need further investigation because, on the basis of the body surface and the plasma cholesterol concentration, one group (214) was able to predict correctly whether a subject was susceptible or resistant to bends in approximately 80% of the laboratory personnel exposed. The body surface, in square meters multiplied by the plasma cholesterol in milligrams percent over 100, gave an index which served as the basis for the predictions. The higher the index, the greater the susceptibility.

Postflight effects of mental depression, fatigue, irritability, etc., have been reported to occur in some individuals (31, 62, 184, 204), but no lasting harmful deterioration resulted (61). The relationship of such complaints as sleeping less soundly, lack of appetite, or tiring more easily, to high altitude exposures has been found difficult to determine (230). A direct experiment on fatigue was performed on 44 subjects who were caused to lose sleep, make 1-hour marches, etc. When this group was exposed to 35,000 feet for 2 hours, there was no increase in the incidence of symptoms (229).

In summary, it appears that some individuals become more susceptible to dysbarism when they have been repeatedly exposed to high altitudes, but others become more resistant. Most persons demonstrate no definite change in susceptibility. In individual subjects, the optimal period between exposures is unknown. There may be a correlation between plasma cholesterol and susceptibility to bends, but this is uncertain.

*Miscellaneous Factors*

Apprehension

As has been mentioned previously, the grading of symptoms as tolerable or intolerable is subjective, and the quantitative treatment of such data may not be entirely valid. Individuals who are apprehensive may have a lower threshold for tolerance of symptoms. One study (239) indicates that symptoms are almost

doubled in frequency and the tendency for mild pains to become intensified until they are incapacitating is very greatly increased by apprehension. A group of 100 subjects whose apprehension was purposely exaggerated by psychologic means were then exposed to 35,000 feet and had a 47% incidence of symptoms. A second group of 100 who were psychologically treated so as to reduce apprehension to a minimum had a total incidence of only 28%. In some individuals, apprehension would be reduced by the experience gained on repeated exposures. The apprehension of others might be increased. Theoretically, apprehension should result in some degree of hyperventilation and, hence, the incidence of symptoms reduced. All of this shows that on the basis of one study, it is difficult to conclude that apprehension would be a real factor in producing bends. As indicated above and previously, the quantitative grading of qualitative symptoms may be misleading.

## Race and nationality

Motley et al. (183) have presented data on American white, American Negro, and French cadets who were exposed to 38,000 feet in low pressure chambers. There was a significant difference in the recorded incidence of bends in the three groups. Both the French and the Negro groups had a bends incidence less than the white. All grades of bends were experienced by 5.8% of 1,235 French, 10.4% of 1,284 Negro, and 13.7% of 43,863 white cadets. It seems probable that race pride accounted for much of the difference, because the incidence of grade 4 symptoms was 0.67% for the white, 0.39% for the Negro, and 0.4% for the French. In other words, when better qualitative criteria are present as in grade 4 symptoms, then the data are more valid quantitatively. It was thought, also, that in the case of the French students, language difficulties may have caused a tendency not to report grades 1 and 2 bends. However, the incidence of 4.03, 2.61, and 1.8% grade 3 bends for the white, Negro, and French cadets, respectively, is difficult to account for, except on the basis of race pride causing a marked determination to suffer discomfort sufficient to force descent of individuals not similarly motivated.

## Others

Smoking per se did not predispose to bends; mild illnesses as reported on questionnaires prior to ascent were noncontributory (231).

## Chokes

The term "chokes" as well as "bends" was coined by caisson workers to describe the attacks of dyspnea and sense of oppression in the chest which sometimes resulted when they were decompressed from several atmospheres of pressure. More scientific terminology would be desirable for the aeromedical literature, but these terms are so descriptive that for want of better expressions they have been used extensively.

**Definition.** We may define chokes in aviation as a manifestation of altitude dysbarism usually characterized by several interrelated symptoms:

1. *Substernal distress*, varying from a sense of constriction, tightness or oppression in the chest, to a burning, gnawing, sometimes lancinating pain.

2. *Cough*, which at altitude is usually nonproductive.

*(The substernal distress and cough are aggravated by attempts to take a deep breath.)*

3. *Difficulty in breathing*, which at altitude is accompanied by a sense of suffocation and apprehension.

Actually, there are two types of chokes experienced at altitude. The phenomenon of "true" chokes, with its characteristics as given above, should be differentiated from "throat" or "false" chokes, which is a condition characterized chiefly by cough. Throat chokes is probably due to the aggravation of a pre-existing throat irritation when cold, dry oxygen is breathed at altitude. Although throat chokes may cause embarrassment of respiration, which would be especially important at very high altitude, there are no concomitant chest symptoms.

The symptoms described above are cardinal symptoms of chokes. However, at least one case of "chokes" has been reported to occur at 35,000 feet in an aircraft, in which pain in the chest was not a prominent symptom. The individual had cough, pallor, headache, and then entered a state of neurocirculatory collapse with moderate shock (245). It was questionable that this instance was true chokes rather than a case of hypoxia, with throat irritation. However, borderline cases are to be expected.

**Etiology and mechanism of chokes.** Chokes is thought to be a part of the reflex phenomena resulting from the irritation of pulmonary tissues when gas emboli cause obstruction of pulmonary arterioles and capillaries (32, 42, 43). There has been no direct demonstration of bubbles in the pulmonary vascular bed during an active human case of chokes. However, there are several lines of indirect evidence to support the concept that symptoms of chokes are due to embolism of pulmonary vessels. Roentgenographic plates taken while the subjects were at altitude and manifesting chokes have been diagnosed as showing some enlargement of the right heart (42, 43). This was interpreted to mean that an increased pulmonary resistance could have been due to bubbles, vasoconstriction of pulmonary capillaries, or both. The bubbles themselves, however, were not evident in the plates. Hetherington and Miller (128) have shown that the intravenous injection of nitrogen gas in anesthetized cats, at a rate of 0.1 to 0.6 cc. per minute for periods ranging from 17 to 255 minutes, could produce physiologic effects on the respiratory and circulatory system which simulated the clinical picture of chokes and collapse at altitude and produced various degrees of acute pulmonary pathology. There are many postmortem autopsy findings of bubbles in the right heart and pulmonary bed of caisson workers who succumbed to decompression from increased barometric pressures (133, p. 137). Accidental injection of air during the intravenous administration of fluids to hospital patients commonly produces respiratory and circulatory phenomena. Certainly, there is a tremendous variation in the quantity of air which can be injected intravenously before serious effects are noted. However, this does not mean that merely because there may be few or no effects in some individuals from

even large quantities of intravenous air, the same or other individuals will not show adverse effects when the bubbles lodge in critical areas. In physiologic laboratories many such experiments have been performed on dogs. The amount of air needed to produce effects has varied from 5 cc. to several hundred. One can hear, by means of a stethoscope, the difference in heart sounds even when a readily absorbable gas like oxygen is given intravenously (113). The clinical symptomatology resulting from air introduced intravenously resembles the symptoms of chokes (192).

In this connection, it is reasonable to further indicate that the quantity of air, within certain limits, may not be and probably is not the only important factor. One possible view is that bubbles could "trigger" reflex vasomotor phenomena in susceptible individuals to an extent beyond that which one would expect to see quantitatively from small amounts of bubble stimuli. The presence of air in any hydrostatic system such as the cardiovascular system can and does cause grave physiologic effects. The heart, for example, has valves which are opened and closed by differential hydrostatic pressures developed during the various phases of the cardiac cycle. If the right atrium and right ventricle are attempting to open the auricular-ventricular and pulmonary valves, respectively, by pumping blood which contains bubbles of gas, it is likely that if sufficient bubbles are present, the hydrostatic pressure in these chambers may not reach a value high enough to force the valves. Obviously, there will be interference with circulation of the blood through the lungs, since the frothy blood present in the right ventricle may be incompletely emptied into the pulmonary artery. It appears logical to assume that bubbles which get to the pulmonary vascular bed can cause true embolism with profound reflex effects in some instances. In experiments on guinea pigs, gas bubbles in the blood stream probably did not reach the capillary bed of the lungs but occluded branches of the pulmonary artery. The smallest vessels affected were arterioles of 40 $\mu$ in diameter (86, 87).

Chokes usually occurs on ascent or while at the peak altitude. However, paradoxically, cough may be exacerbated (36) or chokes may appear for the first time during descent from altitude in individuals who had no sign of chokes at altitude (203) but did

have bends. A possible explanation of the above paradoxical cases of chokes may be that the bubbles were present in noncritical areas at the peak altitude but, because of their size, did not move. During descent, these bubbles became smaller and changed their location, moving to more critical or sensitive areas. In doing so, some of them could have caused embolism or produced a pulmonary vascular spasm sufficient to give symptoms of chokes. This mechanism parallels that previously postulated for the occurrences of bends during descent from altitude, except that in the case of chokes, the bubbles are thought to be chiefly intravascular.

Evelyn (69) had postulated that chokes was probably due to the irritation of breathing 100% oxygen because the burning type of chest pain in the respiratory passages suggested pulmonary symptoms of oxygen toxicity. This view would seemingly receive some support from the following observations by Stewart et al. (230). An altitude chamber technician had been suffering from marked substernal irritation and interference with respiration while at 35,000 feet in a low pressure chamber. He discontinued his oxygen supply and the discomfort in his chest disappeared completely during about 1 minute of this severe hypoxia. After resumption of breathing oxygen, he was able to remain at 35,000 feet free of chest symptoms for more than 1 hour. Thirty-seven additional men with chest discomfort at 35,000 feet were instructed to remove their masks and take four ordinary inspirations of air. "This procedure resulted in marked improvement in those who had mild symptoms, some improvement in moderate cases, but very little improvement in most of those with severe symptoms. In most cases, the reduction of the chest discomfort was temporary, but some men were able to remain at 35,000 feet without symptoms for a period of more than one hour."

It is difficult to explain the above observations completely, but the mechanism of chokes cannot logically be ascribed to oxygen irritation, because as Gray (103) has indicated: (a) breathing 100% oxygen at high altitude is not toxic; (b) caisson workers on decompression from 2 or 3 atmospheres develop chokes breathing air; (c) chokes at altitude usually disappears during descent even though 100% oxygen is breathed continuously on descent.

It is very likely that cough without chest symptoms of any type is due to the mucosal drying effects of breathing dry oxygen on a pre-existing pharyngeal or laryngeal irritation. The severe hypoxia caused by removal of oxygen masks at 35,000 feet may have been a counterstimulation sufficient to cause a release of pulmonary vascular spasm or facilitate bubble dissipation. This method of relieving chokes, if it is a method, is obviously dangerous. The observations, however, point up a requirement for further study of the mechanism of chokes.

**Grading and significance of chokes.** The general scheme of grading symptoms of altitude dysbarism into four categories may also be applied to the grading of chokes. Grades 1 and 2 are tolerable and grades 3 and 4 are intolerable requiring descent from altitude or recompression in the cases of caisson workers or divers. Cases of chokes at altitude have been described in several reports which indicate that the condition may be transient or tolerable for several hours (36, 37, 42, 109). On the other hand, instead of developing slowly, severe grades of chokes may develop in the course of just a few minutes. In one series of tests at altitude, the average time required for grades 3 and 4 chokes to cause descent was 6 to 7 minutes (103).

However, regardless of grade and regardless of whether the bubble, angiospasm, agglutination theories, or a combination of several theories is eventually shown to be the important mechanism producing chokes, one fact should be overemphasized rather than the reverse. *True chokes at altitude or on decompression from high barometric pressures should be regarded as a dangerous symptom, the gravity or potential seriousness of which requires immediate recognition and prompt action by the trained individuals in attendance.*

The occurrence of true chokes should suggest to the observers immediately that, because of the interference with respiration, severe hypoxia may result and, because of effects on respiration and the cardiovascular system, collapse may ensue. No case of true chokes should be regarded lightly. All grades are potentially dangerous, even after the individual returns to normal barometric

pressures. For this reason, prolonged observation of the individual may be necessary as ascertained from the subject's condition after return to ground level. As we have seen in the report on "Neurocirculatory Collapse at Altitude," there have been instances of apparent recovery on descent from high altitude only to have the individual progress into secondary shock during a variable period after descent.

It is pertinent to reiterate that the occurrence of true chokes at altitude implies that the individual's body is already demonstrating the effects of a disturbed physiology. It is safer to err on the side of being excessively cautious and think of the condition as dangerous than it is to leave the individual at altitude and risk the condition's becoming very serious. In addition to the physiologic effects, there is often a marked psychologic reaction when the individual experiences symptoms of asphyxiation. As compared to bends, a greater percentage of individuals who develop severe chokes are prone to collapse (205).

**Incidence of chokes.** Among the symptoms of dysbarism which are sufficiently severe to cause descent, chokes is usually second only to bends (106, 211, 217).

In general, the factors which affect the incidence of chokes at altitude are the same as those which affect bends, except that, because of the decreased incidence, the direct relationship of many factors would be difficult to prove statistically.

The altitude attained, duration of exposure, age, obesity, and exercise are definite factors in the occurrence of chokes. Table XIV shows the increased incidence of chokes at increasing altitudes and also the effects of exercise on incidence. The trend is, at best, very general owing to the variable experimental technics, durations of time, and the number of subjects. Incidence appears to be higher in the experiments which have the least number of subjects. The difference in incidence between 35,000 and 38,000 feet would be difficult to determine. Considering the number of subjects, however, differences between altitudes such as 30,000 and 38,000 feet are easily seen.

## TABLE XIV

*Incidence of chokes at altitude*

| Reference | Altitude (ft.) | Total tests | Total incidence | | Chokes causing descent | | Comment |
|---|---|---|---|---|---|---|---|
| | | | No. | % | No. | % | |
| 217 | 20,000 | 1,813 | 24 | 1.3 | 0 | 0 | With exercise |
| 99 | 27,000 | 93 | — | — | 0 | 0 | With exercise |
| 99 | 30,000 | 135 | — | — | 1 | 0.7 | With exercise |
| 202 | 30,000 | 24 | 8 | 33.3 | 2 | 8.5 | 6-hour flight with exercise |
| 202 | 30,000 | 24 | 2 | 8.5 | 0 | 0 | Exercise and 1-hour denitrogenation |
| 99 | 33,000 | 100 | — | — | 0 | 0 | No exercise |
| 99 | 33,000 | 143 | — | — | 3 | 2.1 | With exercise |
| 226 | 35,000 | 118 | 3 | 2.5 | — | — | No exercise, 3-hour flight |
| 226 | 35,000 | 178 | 5 | 2.8 | — | — | No exercise, 2-hour flight |
| 32 | 35,000 | 1,000 | 20 | 2.0 | 7 | 0.7 | With exercise, slow ascent |
| 211 | 35,000 | 584 | 12 | 2.1 | 7 | 1.2 | No exercise |
| 99 | 35,000 | 429 | — | — | 7 | 1.6 | No exercise |
| 99 | 35,000 | 149 | — | — | 4 | 2.7 | With exercise |
| 230 | 35,000 | 3,744 | 165 | 4.4 | 112 | 3.0 | No exercise |
| 106 | 35,000 | 243 | — | 4.4 | 12 | 4.9 | No exercise |
| 97 | 35,000 | 101 | — | — | 5 | 4.95 | No exercise |

## TABLE XIV (Continued)

| Reference | Altitude (ft.) | Total tests | Total incidence | | Chokes causing descent | | Comment |
|---|---|---|---|---|---|---|---|
| | | | No. | % | No. | % | |
| 107 | 35,000 | 723 | — | — | 45 | 6.21 | No exercise |
| 109 | 35-38,000 | 2,920 | 105 | 3.6 | 66 | 2.3 | No exercise |
| 231 | 38,000 | 2,636 | 34 | 1.3 | 11 | 0.4 | No exercise, slow ascent |
| 83 | 38,000 | 1,982 | — | — | 21 | 1.06 | Mild exercise, 1-hour flight |
| 208 | 38,000 | 1,934 | 69 | 3.5 | 36 | 1.8 | No exercise |
| 210 | 38,000 | 6,639 | 162 | 2.44 | 123 | 1.85 | No exercise |
| 83 | 38,000 | 4,524 | — | — | 124 | 2.7 | No exercise, 3-hour flight |
| 83 | 38,000 | 378 | — | — | 11 | 2.9 | No exercise, 3-hour flight |
| 98 | 38,000 | 950 | — | — | 35 | 3.7 | With exercise |
| 36 | 38,000 | 167 | — | — | 7 | 4.2 | With exercise |
| 107 | 38,000 | 283 | — | — | 16 | 5.58 | No exercise, 1- to 3-hour flight |
| 163 | 38,000 | 160 | — | — | 12 | 7.5 | With exercise, 3-hour flight |
| 97 | 38,000 | 101 | — | — | 8 | 7.92 | No exercise, 3-hour flight |
| 142 | 40,000 | 105 | 1 | 1.0 | 1 | 1.0 | No exercise, 1-hour flight |
| 226 | 40,000 | 118 | 18 | 15.2 | 6 | 5.1 | No exercise, 1-hour flight |
| 226 | 40,000 | 178 | 17 | 9.5 | — | — | No exercise, 2-hour flight |
| 142 | 47,500 | 56 | 3 | 5.2 | 1 | 1.7 | No exercise, pressure breathing |

**Symptomatology of chokes.** We have given in the definition of chokes four characteristics or basic criteria for recognizing true chokes which occur at altitude or on decompression from high atmospheric pressures. The severity of symptoms is certainly variable, just as in the case of bends. These symptoms may be intermittent (36) but have a tendency to progress (103).

The *substernal distress* may vary from a dry sensation in the chest (36) to a burning, gnawing, sometimes lancinating substernal pain which does not, in the usual case, radiate to other regions. There may be only a sensation of fullness in the chest, a sense of constriction, tightness, or oppression. Sometimes, the sensation is described as a burning or rawness which is similar to that experienced during strenuous runs or exhaustive exercises in cold weather (71). These symptoms may persist for some time even after return to ground level pressures, and residual chest soreness may persist for hours or days.

The *symptom of cough* varies from a desire to cough, which is controllable, to a distressing paroxysmal cough which interferes with respiration and very probably also with cardiovascular physiology. The latter type of cough is seemingly a chain reaction since the desire to cough is not relieved by coughing, and can persist for several hours after descent from altitude. The cough is a rasping, hacking cough which is usually nonproductive. At least one case with temporary hemoptysis has been reported (230). The latter is not a common symptom of chokes.

At altitude, the *substernal distress and cough are aggravated to a marked degree by attempts to perform physical exercise.* Even attempts to take a deep breath by the seated, nonexercising subject cause a marked increase in chest symptoms and an intense desire to cough.

*The difficulty in breathing* is accompanied by a sense of suffocation and apprehension (103). Breathing is likely to be rapid and shallow in cases of chokes at altitude because of voluntary attempts on the part of the individual to avoid deep breaths which aggravate his chest pain. This rapid, shallow breathing has the

effect of contributing to the hypoxia because of poor lung ventilation. The sense of suffocation, and probably the loss of judgment due to hypoxia, may cause the individual to feel more acutely the restrictive sensations occasioned by wearing an oxygen mask and prompt him to remove the oxygen mask. This is an obviously dangerous procedure at high altitudes.

There are other symptoms associated with chokes which may be mentioned. With the hypoxemia of severe chokes at altitude one might expect to see cyanosis. Some degree of cyanosis may be noted, especially in those individuals whose dyspneic symptoms and cough result in venous engorgement of the face and neck. More often, however, there is an intense pallor in chokes at altitude which is of sufficient degree to mask any cyanotic color. Along with pallor there can be considerable weakness and perspiration. Faintness and actual syncope are not uncommon in the moderate severe grade of chokes. A marked feeling of fatigue after all other symptoms may have disappeared is a common experience during the period following return to normal atmospheric pressures (103).

Chokes must be differentiated from at least two other conditions: (1) Cough arising from a "tickle" or even a raw feeling like that of a sore throat. This cough frequently accompanies a preflight cold or sore throat, but is not especially aggravated by taking a deep breath. The condition may be due to irritating effects of dry oxygen. (2) Chest wall pain which is usually an aching type of pain, lateral rather than substernal, and located in the chest wall itself rather than internally. It is followed by tenderness and subcutaneous swelling which may not appear for several hours postflight and may endure for a day or more. The chest wall pain is thought to be "soft tissue bends," and the swelling is apparently edema because it does not crepitate (103).

Chokes may occur as the only symptom but most often is associated with bends (36, 37, 230). In the individuals who develop both symptoms, chokes usually appears later in flight.

In tests at 35,000 feet for 2 hours, there were 165 cases of chokes in 3,744 man-exposures (230). On 60 of these 165 man-runs, chokes was the only symptom, and in 76% of these 60 men,

chokes was responsible for causing descent. In the remaining 105 man-runs, chokes was associated with other symptoms, 101 of which were bends, or bends in addition to headache, rash, collapse, nausea, and eye symptoms. Two cases of chest discomfort with nausea occurred. It was concluded that chokes was a more disabling symptom than bends, even though less frequent, as referred to previously. Other authors have indicated that chokes is a more potent factor in precipitating syncopal reactions than is bends.

Some individuals are apparently more susceptible to chokes than are others and in repeated exposures will develop chest pains just about as often as they do bends. Chokes has more of a tendency to progress than does bends or other symptoms. In one series (230), 14% of the cases regressed, 44% progressed, and 42% persisted without change. A mild case of chokes which tends to progress does so rather rapidly. The average duration of a moderate attack is often not more than 5 minutes before descent becomes necessary. Severe chest discomfort caused descent in an average of about 1.6 minutes.

### Central Nervous System Symptoms

During the course of exposing many individuals to high altitude for indoctrination, selection, and research purposes, observations and data have been accumulated on symptoms other than bends and chokes. Among the more important symptoms are those referable to the central nervous system.

In general, it can be stated that the neurologic symptoms observed have not differed a great deal from those reported in divers or caisson workers, except that the latter cases have been more severe. Better technics since the early days have greatly reduced the dangers associated with diving operations. In comparing the central nervous system disturbances arising from altitude and those following high pressure exposures, there appear to be two chief differences (26). The first is the rareness of spinal cord involvement in altitude dysbarism, and the second is the rapid amelioration of altitude symptoms when the subject is recom-

pressed. The rareness of spinal cord symptoms may, in part, be because of immediate recompression which can be accomplished easily. The rapid amelioration of symptoms on descent from altitude may be a function of the fact that fewer bubbles are formed and those which do form should be rapidly absorbed since they have a greater carbon dioxide and water content.

Behnke (26) believes that symptoms arising from the spinal cord are chiefly due to impairment of the circulation produced by gas bubbles. This concept is in agreement with most of the literature reviewed on caisson disease (26, 50, 129, 133).

The incidence and severity of central nervous system symptoms in caisson workers were very high in the early days as compared to individuals exposed to altitude.

Keays, quoted by Hill (129), presented data which is of interest. He analyzed 3,692 cases of caisson disease occurring in 10,000 workers an incidence of 36.9%. The incidence in these 10,000 men, on the basis of 557,000 man-shifts, was 0.66% as illness and 0.0035% deaths.

Of the 3,692 cases, the breakdown showed:

| *Symptom* | *Percent* |
|---|---|
| Bends | 88.78 |
| Bends plus local manifestation (edema, subcutaneous emphysema, etc.) | 0.26 |
| Bends plus prostration, pallor, sweating, etc. | 1.26 |
| Central nervous system: | |
| Brain (hemiplegias) | 0.11 |
| Spinal cord: | |
| Sensory, motor, or both | 2.16 |
| Vertigo (staggers) | 5.33 |
| Collapse | 0.46 |
| Chokes | 1.62 |

There were 20 deaths in individuals manifesting various combinations of the above symptoms. In other case histories of caisson disease, visual symptoms, paresis, paralysis, bladder disturbances, etc., have been recorded with a number of instances of permanent

damage (129). In caisson disease or diver's dysbarism, the condition of vertigo was known as "staggers" because the individuals experienced difficulty in walking and were observed to have an ataxic, titubating gait with varying degrees of incoordination. The condition developed is a "subjective" vertigo in which the individual has the sensation that he is rotating rather than an "objective" vertigo in which the surrounding objects seem to rotate about the individual. In most of the data on dysbarism the term *dizziness* has probably included vertigo as well as giddiness and other subjective sensations not due to the same mechanism. In the report on "Neurocirculatory Collapse at Altitude" there are references made to individuals who probably experienced the subjective type of vertigo, although in most cases this symptom was listed in the data as dizziness.

Hill (129) divided the cases of caisson disease manifesting ear difficulties into two types: (1) cases of temporary deafness and vertigo enduring for about 8 to 14 days and caused by nonequalization of pressure on either side of the eardrum. The tympanic membrane may show signs of congestion and there may be hemorrhages from the middle ear and eustachian tube; (2) cases of Meniere's "complex," consisting of vertigo, deafness, and vomiting which might persist indefinitely. Hill thought that these lesions could be produced by air bubbles either in the central tracts of the cochlea, vestibular nerve, or in the internal labyrinth of the ear. Erdman (68) reported that vertigo occurred in 50% of the cases of caisson disease in his series and thought the disturbance was due to bubbles in the labyrinth or cerebellum. The incidence of vertigo reported in data obtained from altitude training units was less than 1%. The incidence of dizziness in 314 cases of neurocirculatory collapse at altitude was 29.2%. Associated symptoms were nausea, vomiting, or both. There are no cases of altitude dysbarism reported in which alterations in equilibrium were permanent. Most cases of "dizziness" have lasted only a few hours postflight, but a few have endured for several days. In low-pressure-chamber tests, vertigo, faintness, etc., are usually associated with symptoms of bends, chokes, or abdominal distress. Some individuals, however, have been forced to descend from altitude with vertigo as the chief symptom. Whether the mechanism is as described by Hill and others remains a question.

The clinical neurologic reactions which can occur at altitude have been classified (39) as:

1. *Disturbances of equilibrium and coordination:*

   Ataxia

   Dysmetria

   Unsteadiness, etc.

   Vertigo

2. *Disturbances of function of large sensory or motor tracts:*

   Hyperesthesia, hypoesthesia

   Hyperalgesia, hypoalgesia

   Weakness of arm or leg

   Numbness

   Tingling

   Paresis

   Paralysis

   Presence of pathologic reflexes

   Visual symptoms, hemianopsia, nystagmus, diplopia

3. *Disturbances of consciousness and cortical function:*

   Amnesia

   Aphasia

   Hallucinosis

   Acute manic behavior

   Disorientation

4. *Disturbances suggestive of meningeal irritative phenomena, increased intracranial pressure, and migraine-like features:*

   Central vomiting

   Headache

   Dizziness

   Photophobia

   Scotoma and defects common to migraine

   Painful eye movements

5. *Disturbances of subcortical mechanisms associated with phenomena of dyskinesia, hyperkinesia, and aphasia:*

Rest[1]

Dyskinesia

Hyperkinesia

Tremor

Blepharospasm

6. *Scattered nervous system disturbances of minor character:*

Scotoma

Urticaria

Neuralgic pains

Blurred vision

Headache

Syncope

Nausea

Generalized weakness

Mental depression

Loss of depth perception

The above classifications should be compared with that contained in the report on neurocirculatory collapse and will be more meaningful when case histories are reviewed.

The symptoms listed may occur singly, but usually more than one is seen. This reveals that the mechanism of central nervous system disturbances must be such that discrete or widely separated areas of the brain can be affected at the same time. A review of case histories favors the conclusion that the occurrence of bubbles causing ischemic hypoxia is the actual mechanism. Motor, sensory, association, cranial, or somatic nerve areas are affected in an unpredictable manner. Catchpole and Gersh (50) have indicated that where the gas emboli lodge is a matter of chance, but for certain possible reasons the susceptibility of the central nervous system varies in its parts. For example, the circulation of the gray matter of the spinal cord is somewhat anastomotic; hence, severe damage is more frequent in the white matter. Also, the

gray matter has been reported to have a greater number of capillaries and, thus, a better blood supply than the white matter. The pathologic lesions found at autopsy in cases to be discussed later may be explained by these views.

The incidence of central nervous system symptoms during exposure to altitude is small. Brown et al. (39) reported an incidence of 0.28% of temporary symptoms in over 40,000 subjects exposed to altitudes ranging from 30,000 to 38,000 feet.

In 500 subjects at altitudes above 33,000 feet, visual symptoms were observed to occur subjectively in 1.8%. Smarting of the eyes and blurring of vision occurred in about 7% of the cases, but these symptoms usually could be traced directly to hypoxia due to a poor mask fit (156).

Visual field defects constituted the majority (4.6%) of neurologic symptoms reported in 852 forced descents from 2,290 man-flights at 35,000 to 38,000 feet. There was one case each (0.1%) of nystagmus, diplopia, and confusion state (109). These findings check fairly well with a 4.2% incidence of visual symptoms occurring in 167 man-runs to 38,000 feet (36). In the latter report, the only other neurologic symptom of higher incidence was dizziness at 7.2%.

In procedures deliberately designed to induce symptoms of bends at 35,000 feet, there were 91 (12%) syncopal reactions in 37 of 51 subjects who made 754 man-flights. A syncopal reaction was defined as one or more of such symptoms as weakness, faintness, dizziness, pallor, sweating, nausea, confusion, or unconsciousness (205). This experiment emphasizes the close association of central nervous system dysfunction with bends and chokes and suggests that the etiologic mechanism is not too dissimilar. This view is supported by the findings that visual disturbances occurred in less than 1% of 16,293 man-runs on 6,566 individuals exposed to high altitude, and that the symptoms occurred almost wholly in individuals who were highly susceptible to other symptoms, such as bends and chokes (230).

As a general summary of this section, the incidence of central nervous system symptoms in individuals exposed to altitude is very small. The symptomatology is variable in type and severity. The greatest majority of symptoms are temporary. In humans there are no records of permanent damage.

The greater part of the discussion of this subject has been included in the report on "Neurocirculatory Collapse at Altitude."

## Skin Disturbances

**Rash and mottling.** Cutaneous discolorations have been reported most frequently in caisson workers or divers, but are not uncommon in altitude dysbarism. In ascents to altitude, Stewart et al. (230) observed rashes in slightly less than 1% of 1,347 individual exposures. Most were associated with bends or chokes. A few individuals were found to be particularly susceptible to rash which occurred in 50% of the exposures, in some instances. Savely (211) reported an individual who developed a patch of pimples or papules across the back of the neck and shoulders each time he ascended to 35,000 feet. The rash was accompanied by itch and pain, but all of these effects disappeared several hours after descent.

The color varies from a light macular or papular erythematous rash to a purple or bluish-red mottling sometimes called a "violet marbling" of the skin. The mottled zones may be demarcated and intensified by adjacent contrasting areas of pallor. In very severe cases there have been small or large areas of petechial hemorrhage or ecchymoses which have been dark red to black in color. Rashes are most often noted in areas which have a large amount of superficial underlying fatty tissue, such as the abdomen, thighs, chest, and occasionally the shoulders and arms. The rash does not necessarily follow the distribution of cutaneous nerves. Sometimes, attention is drawn to the location by the occurrence of itch; in other cases no other skin symptom is present. Statistics are not available to indicate that the incidences of skin symptoms are higher in obese individuals than in those of normal body type, although such a finding might be expected. Areas affected by rash feel warmer to the touch than do surrounding areas.

The mechanism in many cases may be aero-embolism with vascular congestion and stasis in the subcutaneous tissues. A slowed cutaneous blood flow could result in the local cyanotic type of discoloration since there would be an increased amount of reduced hemoglobin in the vascular bed. Dilation of superficial venules and capillaries in some areas, and vasoconstriction in others would, by contrast, enhance the mottled appearance. In one study (230), when pressure was applied to the rash, the blueness was made to disappear but returned gradually after pressure was removed. This was interpreted as meaning that the bluish discoloration was partially due to dilation of the cutaneous vessels and not to frank extravasation of blood. In severe cases there is hemorrhage into the tissues, especially in caisson disease (129). The persistence of the mottled areas depends upon the extent of the pathologic process. Erythematous areas may clear up in a few hours after their initial appearance while, on the other hand, a purpuric area can endure for several days, as can localized areas of residual tenderness in the subcutaneous fat.

It is of interest that mottling of the skin occurred in 8.3% of 314 cases of neurocirculatory collapse at altitude. It has been noted in fatal cases of dysbarism as well as in individuals who have recovered. In any event, *mottling of the skin must be considered a dangerous symptom* because it signifies the presence of aero-embolism of vessels in the subcutaneous tissues, or an effect on the autonomic nervous system, or both. In the presence of skin disturbances, the obvious question arises as to whether more crucial areas will soon become involved or are already being affected. Stewart et al. (230) reported two serious cases of collapse occurring after a very mild attack of pain but a widespread cutaneous reaction. One of the cases terminated fatally with edema of the lungs developing 12 hours after the flight.

**Paresthesias.** Cutaneous paresthesias are a common manifestation of dysbarism. Occasionally, the symptoms can be moderately severe formication, but most often, they are described as an itch pruritus or prickling of the skin. Scratching of the area produces rash, but rash also occurs independently. The itching or prickling is increased on muscular exercise or if the temperature of the low

pressure chamber is high. In a group of 40 technicians who made frequent ascents to altitude, 8 men experienced cutaneous paresthesias frequently, 6 others reported that paresthesias occurred on approximately half their ascents, 17 rarely noted skin sensations, and 9 had never experienced such phenomena (230). In most individuals, only a part of the body is affected, but on occasion the whole body may be involved. Gibson, quoted by Fraser et al. (79), reported that breathing oxygen for 8 hours caused itching of the skin in 2 subjects at ground level. In both cases, the sensation was located about the site of a pre-existing minor skin injury. This brings up the possibility of some individuals being sensitive to high concentrations of oxygen, or perhaps developing a contact dermatitis rash on the face from the oxygen mask.

Sensations of hot or cold waves are not infrequent phenomena at altitude. The legs, back, and arms are most often affected for periods usually lasting only a few minutes. These symptoms are sometimes associated with collapse.

**Edema and crepitation.** Shortly after descent, or on the following day, a few individuals may notice the appearance of mild to marked subcutaneous edema. Stewart et al. (230) cited 3 cases in which symptoms developed on the day after decompression. The edema in one case formed a hard plaque over the front of both thighs; in another, there was a brawny, tender area in the region of the deltoid which, by x-ray, was shown to be localized to the subcutaneous fat pad. In the third instance, marked edema of the scrotum developed following a rash on the anterior abdominal wall. Of some interest, but of extremely low incidence, is the development of an angioneurotic edema postflight.

The occurrence of edema should be differentiated from the superficial aero-emphysema which sometimes appears, especially in and around the wrist joints and fingers, but also in other areas. The latter condition is characterized by the sensation of a definite crepitation when palpated at altitude much the same as the crepitant sensation associated with infection by gas-producing organisms. The subcutaneous bubbles disappear rapidly after descent from altitude, but the affected areas occasionally develop edema with tenderness for 24 to 48 hours.

## Abdominal Symptoms

Abdominal distress of variable degree is extremely common at high altitude. Although "gas pains" and bloating are not usually major causes of incapacitation, they may, under certain conditions, constitute a serious problem. A summary of the available data on abdominal symptoms at altitude has been compiled recently (5).

In 1,729 cadet subjects at Randolph Field exposed to a simulated altitude of 38,000 feet for 2 or more hours, a total of 542 (31.4%) had gastrointestinal symptoms. The symptoms were severe enough to cause descent in 85 cases (4.9%) (table XV).

### TABLE XV

*Characteristics of abdominal symptoms in 1,729 subjects exposed to 38,000 feet*
*(Randolph Field data)*

| | No. | Absolute (%) | Relative (%) | Symptoms with descent | |
|---|---|---|---|---|---|
| | | | | No. | % |
| Total subjects | 1,729 | 100 | — | 85 | 100 |
| Total abdominal symptoms | 542 | 31.3 | 100 | 85 | 100 |
| Abdominal symptoms, no descent | 457 | 26.4 | 84.3 | 0 | 0 |
| Abdominal symptoms with descent | 85 | 4.9 | 15.7 | 85 | 100 |
| Bloating | 269 | 15.6 | 49.6 | 61 | 71.8 |
| Symptoms transient | 268 | 15.6 | 49.6 | 0 | 0 |
| Symptoms intermittent | 78 | 4.5 | 14.4 | 5 | 5.9 |
| Symptoms steady | 112 | 6.5 | 20.7 | 39 | 45.9 |
| Symptoms progressive | 41 | 2.4 | 7.6 | 41 | 48.2 |
| Pain dull | 190 | 10.9 | 35.0 | 34 | 40.0 |
| Pain sharp | 80 | 4.6 | 14.5 | 51 | 60.0 |
| Symptoms, grade 1 | 342 | 19.8 | 63.1 | 0 | 0 |
| Symptoms, grade 2 | 115 | 6.6 | 20.9 | 0 | 0 |
| Symptoms, grade 3 | 64 | 3.7 | 11.8 | 64 | 75.3 |
| Symptoms, grade 4 | 21 | 1.2 | 3.9 | 21 | 24.7 |

In 99.1% of cases, the gastrointestinal symptoms were located deep in the abdomen (table XVI). With approximately equal frequency, the distress was either generalized throughout the abdomen, restricted to the upper abdomen, or restricted to the lower abdomen. It is probable that the two most frequently involved portions of the gastrointestinal tract, either separately or together, are the stomach and colon.

As shown in table XV, most of the abdominal symptoms are relatively mild and transient, tending to disappear during the stay at altitude (i.e., grade 1). The most common complaint is bloating or distention. Actual pain is less common; and severe, persistent,

## TABLE XVI

*Anatomic distribution of abdominal symptoms (Randolph Field data)*

| | Symptoms—no descent | | Symptoms with descent | |
|---|---|---|---|---|
| | No. | % | No. | % |
| Total abdominal symptoms | 542 | 100 | 85 | 100 |
| Deep in abdomen | 537 | 99.1 | 85 | 100 |
| Superficial | 5 | 0.9 | 0 | 0 |
| Generalized | 151 | 27.8 | 24 | 28.2 |
| Upper abdomen | 154 | 28.4 | 26 | 30.6 |
| (a) Generalized upper | 119 | 22.0 | 20 | 23.5 |
| (b) Upper right | 11 | 2.0 | 4 | 4.8 |
| (c) Upper left | 10 | 1.9 | 2 | 2.4 |
| (d) Upper center | 2 | 0.4 | 0 | 0 |
| (e) Upper right and left | 2 | 0.4 | 0 | 0 |
| Lower abdomen | 160 | 29.5 | 25 | 29.4 |
| (a) Generalized lower | 126 | 23.2 | 19 | 22.3 |
| (b) Lower right | 12 | 2.1 | 1* | 1.2 |
| (c) Lower left | 12 | 2.1 | 2 | 2.4 |
| (d) Lower center | 6 | 1.0 | 3 | 3.6 |
| (e) Lower right and left | 4 | 0.8 | 0 | 0 |
| Center of abdomen | 77 | 14.2 | 10 | 11.8 |
| Left side upper and lower | 5 | 0.9 | 0 | 0 |

*Anatomic defect—hernia present.

colicky pain is relatively uncommon. On the basis of severity, four grades of distress are arbitrarily recognized (table XV). Nausea and vomiting are relatively rare, even in grade 4. A more common accompaniment is a generalized vasomotor reaction manifested by pallor, sweating, and faintness. Abdominal symptoms alone may be responsible for such a syncopal reaction (205).

Gastrointestinal symptoms occur early in a flight, beginning either during ascent or within the first 5 minutes at altitude (107). Nonincapacitating symptoms are usually transient, but may be intermittent or steady. Incapacitating distress usually begins as bloating followed by sharp or dull pain which becomes progressively worse. These symptoms almost always disappear promptly on descent, most being completely relieved at about 22,000 feet. Occasionally, however, residual soreness may persist for 24 hours. It is a frequent observation that the passage of gas per os or per anus at altitude often results in the immediate relief of pain and in the disappearance of all abdominal symptoms within 10 to 15 minutes.

Although a great number of altitude chamber flights have been conducted during the past several years for classification, indoctrination, and research purposes, much of the data so obtained is unsatisfactory for an analysis of abdominal complaints. This is because, in many cases, abdominal symptoms are included with certain other manifestations under miscellaneous effects, and incomplete data are given. Nevertheless, certain factors which appear to influence the incidence and severity of abdominal distress at altitude may be considered. These may be conveniently divided into "flight" factors and "human" factors.

### Flight factors

*Altitude.* In table XVII, data from several sources are arranged in the order of increasing peak altitudes. In general, it is apparent that the incidence of abdominal symptoms increases with increasing altitude. The comparison would, of course, be more satisfactory if all of the experiments tabulated had been conducted under uniform conditions. In spite of certain variations in procedure,

## TABLE XVII

*Incidence of abdominal symptoms with increasing altitude*

| Reference | Altitude (ft.) | Time at altitude (hr.) | Average rate of ascent (ft./min.) | No. of man-tests | Total abdominal symptoms Col. 1 | | Abdominal symptoms no descent Col. 2 | | Abdominal symptoms with descent | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | No. | % | No. | % | No. | % | |
| 170 | 15,000 | 0.5 | 5,000 | 135 | 0 | 0 | 0 | 0 | 0 | 0 | Demand system $O_2$. |
| 170 | 18,000 | 0.5 | 5,000 | 262 | 0 | 0 | 0 | 0 | 1 | 0.04 | Not known if subject had symptoms before ascent. Pressure breathing. |
| 96 | 23,000 | 2 | 3,000 | 312 | 5 | 1.6 | 5 | 1.6 | 0 | 0 | $O_2$ demand system; exercise every 5 min. |
| 96 | 25,000 | 2 | 3,000 | 128 | 7 | 5.4 | 4 | 3.1 | 3 | 2.3 | $O_2$ demand system; exercise every 10 min. |
| 96 | 27,000 | 2 | 3,000 | 93 | 3 | 3.2 | 3 | 3.2 | 0 | 0 | $O_2$ demand system; exercise every 15 min. |
| 96 | 30,000 | 2 | 3,000 | 135 | 0 | 0 | 0 | 0 | 2 | 1.5 | $O_2$ demand system; exercise every 15 min. |

## TABLE XVII (Continued)

| Reference | Altitude (ft.) | Time at altitude (hr.) | Average rate of ascent (ft./min.) | No. of man-tests | Total abdominal symptoms Col. 1 | | Abdominal symptoms no descent Col. 2 | | Abdominal symptoms with descent | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | No. | % | No. | % | No. | % | |
| 96 | 35,000 | 2 | 3,000 | 143 | 0 | 0 | 0 | 0 | 1 | 0.7 | $O_2$ demand system; exercise every 15 min. |
| 7 sets of data (32, 99, 106, 107, 205, 211, 248) | 35,000 | 2 | 1,500-5,000 | 3,731 | 494 | 26.5 | 456 | 24.5 | 90 | 2.4 | Col. 1 and 2 are average of 3 sets of data. |
| 6 sets of data (36, 100, 104, 110, 127, 140) | 38,000 | 1.8 | 3,810 | 1,188 | 246 | 20.7 | 200 | 16.8 | 46 | 3.9 | Col. 1 and 2 from 6 sets of data. |
| 142 | 40,000 | 1.0 | 5,000 | 105 | 33 | 32 | 33 | 32 | 0 | 0 | Cont. flow of $O_2$ |
| 170 | 43,500 | 0.25 | 1,000 | 80 | 0 | 0 | 0 | 0 | 7 | 8.7 | 8" cont. pressure. |
| Randolph Field data | 45,000 | 0.5 | 1,000 | 74 | 24 | 32.4 | 18 | 24.3 | 6 | 8.1 | 8" cont. pressure. |
| 170 | 45,600 | 0.5 | 1,100 | 50 | 0 | 0 | 0 | 0 | 10 | 20.0 | 8" cont. pressure. |
| 142 | 47,500 | 1.0 | 3,000 | 50 | 28 | 54 | 25 | 50 | 3 | 5.3 | 8-10" intermittent pressure. |

## TABLE XVIII

*Effect of rate of ascent on incidence of abdominal symptoms at 38,000 feet*

| Reference | Time at altitude (hr.) | Average rate of ascent (ft./min.) | No. of man-tests | Total abdominal symptoms | | Abdominal symptoms no descent | | Abdominal symptoms with descent | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | No. | % | No. | % | No. | % |
| 173* | Variable | 600 | 16,035 | 1,165 | 7.3 | 862 | 5.4 | 303 | 1.9 |
| 169 | 2 | 1,000 | 180 | — | — | — | — | 7 | 3.9 |
| 98 | 2 | 1,500 | 900 | — | — | — | — | 21 | 2.3 |
| 107 | 2 | 3,000 | 56 | — | — | — | — | 2 | 3.5 |
| 127 | 1.5 | 3,100 | 158 | 46 | 28.9 | 38 | 24.1 | 8 | 4.8 |
| 251 | 1.5 | 3,400 | 29 | 3 | 10.4 | 2 | 6.9 | 1 | 3.5 |
| (98, 101) | 2-3 | 4,000 | 950 | — | — | — | — | 32 | 3.4 |
| (100, 110) | 2 | 4,000 | 443 | 54 | 12.2 | 32 | 7.2 | 22 | 5.0 |
| (143) | 2 | 5,000 | 538 | 96 | 17.8 | 88 | 16.1 | 8 | 1.7 |

*Approximately 60 minutes to reach 38,000 feet; various indoctrinations at 8,000, 10,000, 19,000, 25,000, 30,000 feet; at 38,000 feet for a short time (?) usually.

however, the tendency for abdominal symptoms to occur more frequently at higher altitudes is apparent.

*Rate of Ascent.* In table XVIII, eleven sets of data for flights to 38,000 feet are arranged in order of increasing ascent rate. Except for data of Henry et al. (127), the incidence of total abdominal symptoms appears to increase with increasing ascent rate, but the effect is not striking. There appears to be no effect on the incidence of incapacitating symptoms. Blair et al. (33) have reported no difference in the incidence of symptoms at ascent rates from 2,000 to 5,000 feet per minute.

In this connection, the occurrence of abdominal symptoms following explosive decompression should be pertinent. It has been reported that only 1 of 10 subjects explosively decompressed to 45,000 to 50,000 feet experienced severe gas pains (232). Edelmann et al. (65) did not note an unusual number of severe abdominal symptoms in several hundred subjects explosively decompressed through a range of pressures of 2 to 21 p.s.i. per second. This would be equivalent to changing the simulated altitude from 8,000 to 35,000 feet in from 4.0 to 0.3 seconds. It should be noted, however, that of 709 tests on animals, one guinea pig died of peritonitis due to a ruptured stomach which occurred after 6 explosive decompressions at a rate of 1,124 mm. Hg per second (256).

### Human factors

*Age.* Table XIX summarizes the relationship between age and incidence of abdominal symptoms in 4,423 subjects exposed to an altitude of 38,000 feet for 1 to 3 hours. Although the correlation is not so striking as for bends, the incidence of symptoms does appear to increase with age. If the subjects are divided into two age classes, the incidence of total abdominal symptoms, 33.4%, in the older age group (28 to 47) is considerably and significantly higher than that in the younger group (18 to 27), 20.8% ($P < .0005$). The incidence of incapacitating symptoms is not significantly different in the two groups.

## TABLE XIX

*Distribution of abdominal symptoms in two age groups (Randolph Field data, 38,000 feet)*

| Age | Total abdominal symptoms | | Abdominal symptoms no descent | | Abdominal symptoms with descent | | No. of subjects |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| 18 | 60 | 20.3 | 50 | 16.9 | 10 | 3.4 | 295 |
| 19 | 102 | 16.5 | 82 | 13.3 | 20 | 3.2 | 617 |
| 20 | 129 | 20.3 | 116 | 18.3 | 13 | 2.0 | 634 |
| 21 | 103 | 20.5 | 90 | 17.9 | 13 | 2.6 | 503 |
| 22 | 87 | 21.3 | 76 | 18.6 | 11 | 2.7 | 408 |
| 23 | 67 | 17.3 | 52 | 13.4 | 15 | 3.9 | 388 |
| 24 | 74 | 25.1 | 66 | 22.4 | 8 | 2.7 | 295 |
| 25 | 53 | 18.8 | 46 | 16.3 | 7 | 2.5 | 282 |
| 26 | 72 | 29.9 | 64 | 26.6 | 8 | 3.3 | 241 |
| 27 | 70 | 26.3 | 66 | 24.8 | 4 | 1.5 | 266 |
| Total | 817 | 20.8 | 708 | 18.0 | 109 | 2.8 | 3,929 |
| 28 | 42 | 35.6 | 40 | 33.9 | 2 | 1.7 | 118 |
| 29 | 16 | 28.1 | 13 | 22.8 | 3 | 5.3 | 57 |
| 30 | 18 | 45.0 | 16 | 40.0 | 2 | 5.0 | 40 |
| 31 | 14 | 28.6 | 14 | 28.6 | 0 | 0.0 | 49 |
| 32 | 17 | 24.3 | 15 | 21.4 | 2 | 2.9 | 70 |
| 33 | 9 | 18.7 | 7 | 14.6 | 2 | 4.1 | 48 |
| 34 | 13 | 44.8 | 12 | 41.4 | 1 | 3.4 | 29 |
| 35 | 8 | 38.1 | 7 | 33.3 | 1 | 4.8 | 21 |
| 36 | 7 | 46.7 | 5 | 33.3 | 2 | 13.4 | 15 |
| 37 | 7 | 58.3 | 6 | 50.0 | 1 | 8.3 | 12 |
| 38-47 | 14 | 40.0 | 11 | 31.4 | 3 | 8.6 | 35 |
| Total | 165 | 33.4 | 146 | 29.6 | 19 | 3.8 | 494 |
| Grand total | 982 | 22.2 | 854 | 19.3 | 128 | 2.9 | 4,423 |

*Weight.* Table XX shows the relationship between weight and the incidence of abdominal symptoms in the same group of subjects. Again, there appears to be an increase in the incidence of total symptoms in the heavier classes. When the subjects are divided into two weight classes, the incidence of total abdominal symptoms in the heavier group (160 to 200 + pounds), 24.2%, is slightly, but apparently significantly, higher than that in the lighter group

## TABLE XX

*Distribution of abdominal symptoms according to weight (Randolph Field data)*

| Weight (lb.) | Total abdominal symptoms | | Abdominal symptoms no descent | | Abdominal symptoms with descent | | No. of subjects |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| 120-9 | 20 | 21.0 | 17 | 17.9 | 3 | 3.1 | 95 |
| 130-9 | 71 | 19.9 | 64 | 17.9 | 7 | 2.0 | 356 |
| 140-9 | 166 | 21.4 | 144 | 18.5 | 22 | 2.9 | 777 |
| 150-9 | 215 | 19.7 | 185 | 16.9 | 30 | 2.8 | 1,092 |
| Total | 472 | 20.3 | 410 | 17.7 | 62 | 2.6 | 2,320 |
| 160-9 | 205 | 23.0 | 181 | 20.3 | 24 | 2.7 | 889 |
| 170-9 | 166 | 23.3 | 143 | 20.1 | 23 | 3.2 | 711 |
| 180-9 | 84 | 26.0 | 77 | 23.8 | 7 | 2.2 | 323 |
| 190-9 | 35 | 26.3 | 25 | 18.8 | 10 | 7.5 | 133 |
| 200+ | 20 | 42.5 | 18 | 38.3 | 2 | 4.2 | 47 |
| Total | 510 | 24.2 | 444 | 21.1 | 66 | 3.1 | 2,103 |
| Grand total | 982 | 22.2 | 854 | 19.3 | 128 | 2.9 | 4,423 |

(120 to 159 pounds), 20.3% ($P < .002$). Most of the difference appears to be due to the rapid increase in incidence in individuals weighing over 180 pounds.

*Distribution of the two age classes in relation to the two weight classes*

| | *Age class I (18-26)* | *Age class II (26-47)* |
|---|---|---|
| Weight class I (120-159) | 2,084 | 236 |
| Weight class II (160-200+) | 1,845 | 258 |

Although the heavier weight class contains a significantly greater proportion of older individuals, indicating a significant correlation between weight and age in the group studied, the absolute magnitude of this difference in distribution does not appear to be great enough to account for the observed difference in the incidence of symptoms on the basis of age alone. In other words, increasing age and increasing weight independently are associated with an increased incidence of symptoms.

*Sex.* The influence of this factor cannot be evaluated on the basis of available data. However, as Gray (103) and others have noted, female subjects commonly have severe abdominal distress at altitude unless they are convinced that the social amenities need not be observed and that the passage of gas usually affords relief from distress.

*Quantity of Gas in Intestinal Tract.* X-ray studies have shown that although the quantity of gas in the intestine may be a major factor in the production of abdominal distress at altitude, it is not the only factor. Thus, large quantities may be present in subjects who have no distress and smaller quantities may be seen in those who have fairly severe symptoms (174). In one study at 38,000 feet, there was no consistent correlation between the amount of gas present on x-ray and the occurrence of incapacitating symptoms, except when the gas was present in the ileum (33). On the contrary, Tillisch (241) believes that such a correlation exists. It is not surprising that such differences exist, because—(1) the volume of gas measured by x-ray is an approximation only; (2) probably more important, the sensitivity and motility of the intestinal tract as well as the degree of distention are of obvious importance in determining the presence or absence of symptoms.

*Anatomic Site of Gas Pocketing.* According to x-ray studies, gas in the lower ileum or upper colon caused a high incidence of symptoms at 37,000 feet (33). The addition of 500 cc. of air to the stomach resulted in slight to severe pain at altitude in 7 of 15 subjects; the same quantity added to the duodenum caused incapacitating abdominal pain in 8 of 13 subjects, and some distress in all 13; severe distress occurred below 30,000 feet and incapacitating distress above this altitude. These authors found a consistent relationship between incapacitating pain and the quantity of gas in the ileum, but the relationship was inconsistent for other tests.

*Diet.* Three types of dietary factors may be important in abdominal distress at altitude: (1) the so-called "gas-forming" foods which may contribute to the volume of gas present at sea level; (2) foods which contain gastrointestinal irritants; and (3) foods to which the individual may manifest an allergic reaction.

Blair et al. (33) found that the so-called gas-forming foods were not associated with an unusual incidence of distress at altitude. Although the volume of abdominal gas was not uniformly influenced by diet, these authors did find that high carbohydrate meals were most likely to increase the volume. Flights taken after two successive high carbohydrate meals were associated with a higher incidence of abdominal distress than those following high protein meals. In this same study, carbonated water and melons were consistently found to produce gastrointestinal symptoms at altitude. Kantor and Marks (153), however, maintain that $CO_2$ ingested in carbonated beverages is either quickly belched or rapidly absorbed, even from the stomach and, hence, is not likely to cause flatulence. These observations, however, applied to patients at ground level. In a recent study (42), the incidence of abdominal distress in 7 subjects repeatedly exposed to an altitude of 38,000 feet appeared to be increased on a high carbohydrate diet, relatively unchanged on a high protein diet, and decreased on a high fat and Larkin-Watt diet (see table XXI).

Alvarez (7) believes that melons, beans, cabbage, peanuts, peppers, and cucumbers contain a gastrointestinal irritant substance. Tillisch (241) found that subjects given an irritating diet and exposed to 38,000 feet 3 hours later showed no more gas on x-ray either at ground level or at altitude than they did on a bland diet. In spite of this, however, there was an increased incidence of abdominal distress on the irritating diet. This is another illustration of the fact that alterations in the sensitivity and motility of the intestinal tract are as important as the amount of gas present in determining the presence or absence of abdominal symptoms. The temperature of the ingested food may be important as it is known that some individuals bloat suddenly when they take ice cold fluid into an empty stomach (8). According to one report (127), the incidence of abdominal symptoms was thought to be higher in flights taken 3 hours after a meal than in those taken 1 to 2 hours post cibum. This may be related to the observation of Woodyatt and Graham (259) that in many hyperchlorhydric patients, eructation occurs most frequently about 3 hours after meals.

## TABLE XXI

*Incidence of abdominal symptoms of 7 subjects repeatedly exposed to altitude (42, 142)*

| | Altitude (ft.) | Time at alt. (hr.) | Average rate of ascent (ft./min.) | No. of man-tests |
|---|---|---|---|---|
| Control—no exercise | 38,000 | 2 | 5,000 | 97 |
| Control with exercise every 10 minutes at altitude | 38,000 | 2 | 5,000 | 218 |
| High fat diet with exercise | 38,000 | 2 | 5,000 | 55 |
| High protein diet with exercise | 38,000 | 2 | 5,000 | 92 |
| High carbohydrate diet with exercise | 38,000 | 2 | 5,000 | 76 |
| Larkin and Watt diet† | 38,000 | 2 | 5,000 | 69 |
| 1-hour denitrogenation, ground level | 38,000 | 2 | 5,000 | 53 |
| Intermittent pressure breathing 8" $H_2O$ | 38,000 | 2 | 5,000 | 70 |
| Control—no exercise | 40,000 | 1 | 5,000 | 105 |
| Intermittent pressure breathing 8-11" $H_2O$ | 47,500 | 1 | 5,000 | 50 |

*Not included as part of total symptoms.

†10,000 units vitamin D, 15 gr. Ca lactate, 7.5 gm. NaCl, 2 qt. milk/day; continuous flow of $O_2$ used from ground level in all tests except those with intermittent pressure breathing.

There is abundant clinical evidence pointing to gastrointestinal allergy as a cause of edema, inflammation, and altered irritability and motility of the gastrointestinal tract (7). No specific studies have been made relating gastrointestinal allergy to abdominal distress at altitude, but such a factor, if present, would obviously be expected to contribute to distress.

It is obvious from the complexity of dietary and other factors that no simple instructions may be given to flying personnel regarding diet. As Gray (103) has stated: "We tell flying personnel that if they have any abdominal distress before a flight to high

## TABLE XXI (Continued)

| Total abdominal symptoms | | Abdominal symptoms no descent | | Abdominal symptoms with descent | | Belching* | | Flatulence* | |
|---|---|---|---|---|---|---|---|---|---|
| No. | % | No. | % | No. | % | No. | % | No. | % |
| 20 | 20.6 | 19 | 19.6 | 1 | 1.0 | 74 | 76.2 | 73 | 75.2 |
| 32 | 14.6 | 29 | 13.3 | 3 | 1.3 | 113 | 51.8 | 188 | 83.9 |
| 3 | 5.4 | 3 | 5.4 | 0 | 0 | 43 | 78.3 | 45 | 81.9 |
| 16 | 17.6 | 14 | 15.4 | 2 | 2.17 | 58 | 64.1 | 79 | 85.0 |
| 25 | 32.8 | 23 | 30.2 | 2 | 2.6 | 67 | 86.2 | 73 | 96.2 |
| 7 | 10.1 | 7 | 10.1 | 0 | 0 | 51 | 74.0 | 67 | 97.2 |
| 7 | 13.2 | 5 | 9.4 | 2 | 3.8 | 24 | 45.3 | 25 | 47.2 |
| 10 | 14.3 | 9 | 12.9 | 1 | 1.4 | 42 | 60.0 | 52 | 74.3 |
| 33 | 32.0 | 33 | 32.0 | 0 | 0 | 84 | 80.0 | 84 | 80.0 |
| 28 | 54.0 | 25 | 50.0 | 3 | 5.3 | 50 | 100.0 | 50 | 100.0 |

altitudes, it will in all probability get worse and not better on reaching altitude. With respect to diet we tell them that if they know from their own experience that any particular foods cause them trouble, they should avoid them when possible."

*Alcoholic Beverages.* Occasionally, a subject will ascribe his abdominal distress at altitude to the ingestion of beer or whiskey during the 24-hour period prior to ascent. In this connection, there is experimental evidence that alcohol in quantity can alter the motility of the colon in the dog and in man for several hours after ingestion, but it has not been proved that these effects

would endure as long as 12 to 24 hours (4). Clinically, however, it is recognized that gastrointestinal upsets are quite common 12 to 24 hours after ingestion of large quantities of alcohol, depending upon the individual differences in capacity and tolerance. There are several studies which provide data on the effect of alcohol on abdominal distress at altitudes. According to one study (33), the ingestion of beer the night before ascent not only failed to increase the incidence of abdominal distress at altitude, but actually appeared to decrease it.

Data obtained at Randolph Field are summarized in table XXII. These tests were made on cadets exposed to 38,000 feet for 2 to 4 hours. In contrast to the results quoted previously, these data show a statistically significant increase ($P < .01$) in the total incidence of abdominal symptoms in those subjects who had partaken of either liquor or beer during the previous 24 hours. The incidence of incapacitating abdominal symptoms was not significantly different in the three groups.

## TABLE XXII

*Effect of alcoholic beverages on incidence of abdominal symptoms at 38,000 feet (rate of ascent 4,000 ft./min.) (Randolph Field data)*

| | No alcohol in previous 24 hours | | Liquor—3 oz. or more | | Beer—2 bottles or more | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| Number of subjects | 1,493 | 100 | 108 | 100 | 128 | 100 |
| Number with no abdominal symptoms | 1,052 | 70.5 | 64 | 59.2 | 71 | 55.6 |
| Total with abdominal symptoms* | 441 | 29.5 | 44 | 40.8 | 57 | 44.4 |
| (a) Abdominal symptoms—no descent | 369 | 24.7 | 40 | 37.1 | 48 | 37.4 |
| (b) Abdominal symptoms—with descent | 72 | 4.8 | 4 | 3.7 | 9 | 7.0 |

*Bloating, distention with distress or pain, and descents due to gas.

*Drugs.* In an attempt to reduce the incidence of abdominal symptoms at altitude, both stimulatory and inhibitory gastrointestinal drugs have been tried without success. Among those tried have been a mixture of Prostigmine and atropine, and such "antispasmodics" as Pavatrine and Metropine (33). If they had any effect at all, these drugs appeared to increase rather than decrease the amount of abdominal pain at altitude. It has been noted in controlled colon motility studies (2) that if propulsive waves reach a segment which contains gas or other material, and if the segment does not respond in a synergistic manner by "accepting" the wave, a mild to strong cramp-like sensation may be felt. Prostigmine, by increasing propulsive colon motility (3), could exacerbate this mechanism, especially at altitude, since the exaggerated motility would be acting on expanded gas.

*Denitrogenation.* This procedure is highly effective in preventing bends and chokes at altitude and, conceivably, might be of some value in the prevention of abdominal symptoms. Table XXIII summarizes data from several sources regarding the effect of denitrogenation on abdominal distress at altitude.

The only study in this group which was specifically concerned with abdominal symptoms is that of Henry et al. (127). In this study, all subjects ate in a common mess hall, and other factors were controlled so that the results should be reliable. The data so obtained show a significant (although small) reduction in the total incidence of abdominal symptoms after 51 minutes of denitrogenation ($.02 < P < .05$), and a considerable significant reduction after 111 minutes ($P < .003$). The observed reduction in the incidence of incapacitating symptoms to zero after 111 minutes of denitrogenation is also probably significant ($.05 < P < .08$).

Ivy's data (143) shows a reduction in the incidence of total abdominal symptoms from 20.6% to 13.2% following 60 minutes' denitrogenation. Although this difference is not statistically significant ($P > .05$), it is of the same order of magnitude as Henry's observations and would probably prove to be significant if more cases were studied. Abdominal symptoms which caused descent were slightly increased.

## TABLE XXIII

*Effect of denitrogenation for various periods of time on incidence of abdominal symptoms at 38,000 feet*

| Reference | Time at altitude (hr.) | Average rate of ascent (ft./min.) | No. of man-tests | Total abdominal symptoms | | Abdominal symptoms no descent | | Abdominal symptoms with descent | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | No. | % | No. | % | No. | % | |
| 6 sets of data (36, 100, 104, 110, 127, 251) | 1.8 | 3,810 | 1,188 | 246 | 20.7 | 200 | 16.8 | 46 | 3.9 | Control values—no denitrogenation |
| 127* | 1.5 | 3,100 | 158 | 46 | 28.9 | 38 | 24.1 | 8 | 4.8 | 100% $O_2$ at 10,000 ft. + exercise (control) |
| | 1.5 | 3,100 | 68 | 16 | 23.2 | 14 | 20.3 | 2 | 2.9 | 12-min. denitrogenation + exercise |
| | 1.5 | 3,100 | 68 | 13 | 19.2 | 10 | 15.1 | 3 | 4.1 | 15-min. denitrogenation + exercise |
| | 1.5 | 3,100 | 62 | 6 | 9.8 | 6 | 9.8 | 0 | 0 | 111-min. denitrogenation + exercise |
| 42 | 2.0 | 5,000 | 97 | 20 | 20.6 | 19 | 19.6 | 1 | 1.0 | Control—no exercise or denitrogenation |
| | 2.0 | 5,000 | 218 | 32 | 14.6 | 29 | 13.3 | 3 | 1.3 | Control with exercise; no denitrogenation |
| | 2.0 | 5,000 | 53 | 7 | 13.2 | 5 | 9.4 | 2 | 3.8 | 60-min. denitrogenation at ground level |
| Randolph Field data | 2.3 | 3-4,000 | 1,729 | 542 | 31.2 | 457 | 26.4 | 85 | 4.9 | Control values; no denitrogenation control |

## TABLE XXIII (Continued)

| Reference | Time at altitude (hr.) | Average rate of ascent (ft./min.) | No. of man-tests | Total abdominal symptoms | | Abdominal symptoms no descent | | Abdominal symptoms with descent | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | No. | % | No. | % | No. | % | |
| 104 | 2 | 4,000 | 76 | 17 | 22.4 | 13 | 17.1 | 4 | 5.3 | Control automix to 25,000 feet |
| | 2 | 4,000 | 87 | 19 | 21.9 | 16 | 18.4 | 3 | 3.5 | 45-min. denitrogenation |
| | 2 | 4,000 | 88 | 14 | 15.9 | 12 | 13.6 | 2 | 2.3 | 45-min. denitrogenation with exercise |
| 101 | 2 | 4,000 | 204 | — | — | — | — | 4 | 2.0 | 15-min. denitrogenation ground level |
| | 2 | 4,000 | 145 | — | — | — | — | 9 | 6.2 | 30-min. denitrogenation ground level |
| | 2 | 4,000 | 180 | — | — | — | — | 5 | 2.8 | 45-min. denitrogenation ground level |
| 98 | 2 | 1,500† | 181 | — | — | — | — | 1 | 0.5 | 15-min. denitrogenation 15,000 feet |
| | 2 | 1,500 | 205 | — | — | — | — | 7 | 3.3 | 15-min. denitrogenation 20,000 feet |
| | 2 | 1,500 | 290 | — | — | — | — | 8 | 2.7 | 15-min. denitrogenation 25,000 feet |
| | 2 | 1,500 | 224 | — | — | — | — | 5 | 2.2 | 15-min. denitrogenation 30,00 feet |

*Experiments specifically designed to study effect of denitrogenation on abdominal symptoms.

†Rate of ascent is 4,000 ft./min. between ground and 15,000 ft., ground and 20,000 ft., etc.

Gray's data fails to show any significant effect from 45 minutes of denitrogenation on the total incidence of symptoms. The occurrence of only one case of incapacitating abdominal symptoms in 181 tests following 15 minutes' denitrogenation at 15,000 feet may be related more to the delay in reaching altitude than to the denitrogenation.

In summary, denitrogenation, if carried on long enough, appears to reduce the total incidence of abdominal distress at altitude, but the reduction is not as marked and requires a longer period than a similar prophylaxis for bends and chokes. The incidence of incapacitating abdominal symptoms is not significantly altered by this procedure.

*Exercise.* It is difficult to determine the effect of exercise on the incidence of abdominal symptoms at altitude from the data available; first, because there are few comparable sets of data with and without exercise, and second, because the exercise was not usually begun until 5 to 10 minutes after reaching peak altitude and most abdominal symptoms begin earlier than this. Data from experiments in which incidental observations were made on this point have been assembled in table XXIV.

The only directly comparable data appears to be that of Ivy et al. (143), and this shows a reduction in the total incidence of abdominal symptoms from 26.6% in the nonexercise group to 14.6% in the exercise group, a difference which is not statistically significant ($P > .15$).

If the total for all of the tests with exercise is compared with the total for those without exercise, the incidence of total abdominal symptoms is 27.1% in the former and 13.7% in the latter. Note, however, that this high value in the exercise group is determined largely by the extraordinarily high incidence of 44.3% reported by Bridge et al. (36).

In summary, the available data do not permit any conclusions regarding the effects of exercise on abdominal distress at altitude. Theoretically, one might expect either a beneficial effect due to

## TABLE XXIV

*Effect of exercise at 38,000 feet on incidence of abdominal symptoms*

| Reference | Time at altitude (hr.) | Average rate of ascent (ft./min.) | No. of man-tests | Total abdominal symptoms | | Abdominal symptoms no descent | | Abdominal symptoms with descent | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | No. | % | No. | % | No. | % | |
| 127 | 1.5 | 3,100 | 158 | 46 | 28.9 | 38 | 24.1 | 8 | 4.8 | Exercise every minute |
| 36 | 1.5 | 3,170 | 167 | 74 | 44.3 | 67 | 40.1 | 7 | 4.2 | 10 step-ups every minute |
| 251 | 1.5 | 3,400 | 29 | 3 | 10.4 | 2 | 6.9 | 1 | 3.5 | 5 knee bends + arms extended with weights every 10 min. |
| 42 | 2.0 | 5,000 | 218 | 32 | 14.6 | 29 | 13.3 | 3 | 1.3 | Knee bends + arms extended with weights every 10 min. |
| Total | | | 572 | 155 | 27.1 | 136 | 23.8 | 19 | 3.3 | All tests with exercise |
| 100 | 2.0 | 4,000 | 239 | 31 | 13.0 | 19 | 8.0 | 12 | 5.0 | No exercise |
| 110 | 2.0 | 4,000 | 204 | 23 | 11.4 | 13 | 6.4 | 10 | 4.9 | No exercise |
| 42 | 2.0 | 5,000 | 97 | 20 | 26.6 | 19 | 19.6 | 1 | 1.0 | No exercise |
| Total | | | 540 | 74 | 13.7 | 51 | 9.4 | 23 | 4.3 | Total no exercise |
| 101 | 2.0 | 4,000 | 223 | | | | | 16 | 7.2 | No exercise |
| 98 | 3.0 | 4,000 | 727 | | | | | 22 | 2.9 | No exercise |
| 107 | 1.5 | 2-4,000 | 283 | | | | | 16 | 5.7 | No exercise |
| Grand total | | | 1,773 | | | | | 77 | 4.3 | Grand total no exercise |

the promotion of the expulsion of flatus, or a harmful effect due to an increase in abdominal pressure when the abdominal muscles are contracted.

*Experienced Versus Inexperienced Personnel.* Henry et al. (127) do not believe that adaptation reduces the number of abdominal symptoms on successive flights, because in a series of 80 men exposed twice to 38,000 feet, there was no decrease in the number of abdominal symptoms in the second tests as compared to the first. However, table XXV presents data which tend to show that experienced personnel do have a lower incidence of total abdominal symptoms and abdominal symptoms which cause descent than do inexperienced personnel. Because of the large number of factors entering into production of gas pains at altitude, only a general explanation is possible. Experienced personnel are less apprehensive. Forewarned of their time of ascent, they probably pay more attention to dietary factors and, if ill due to any cause, will postpone their scheduled ascent to another day. In addition, experienced personnel are aware of a few miscellaneous measures, such as emptying bowels, loosening belts and clothing before ascent, massaging abdomen if distress does begin at altitude and, most important, tolerating abdominal symptoms at altitude if not too severe, since in 5 or 10 minutes, passage of gas and belching will relieve most symptoms. In Ivy's experiments, the latter means of assurance was very effective, even with inexperienced personnel, and probably explains the relatively low incidence of descents due to abdominal pain at 40,000 feet (table XVII).

*Anatomic Defects.* In isolated cases anatomic defects may be factors in causing abdominal symptoms. In one instance of right inguinal hernia, severe pain localized to the right lower abdomen occurred before reaching 38,000 feet and caused descent (table XXVI). Similarly, one subject with a history of ruptured appendix was forced to descend with symptoms referable to the center of the abdomen. A third subject with a history of gunshot wound which pierced intestines and bladder had tolerable abdominal symptoms in the location of his operative scar (Randolph Field data).

## TABLE XXV

*Incidence of abdominal symptoms—experienced versus inexperienced personnel*

| Reference | | Altitude (ft.) | Time at altitude (hr.) | Average rate of ascent (ft./min.) | No. of man-tests | Total abdominal symptoms | | Abdominal symptoms no descent | | Abdominal symptoms with descent | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | No. | % | No. | % | No. | % | |
| 211 | (a) | 35,000 | 1.0 | | 363 | | | | | 9 | 2.5 | Reg. personnel of Aeromed. Laboratory |
| | (b) | 35,000 | 1.0 | | 52 | | | | | 4 | 7.7 | Personnel assigned for chamber training |
| | (c) | 35,000 | 1.0 | | 304 | | | | | 8 | 2.6 | Experienced flight personnel |
| 100 | (a) | 38,000 | 2.0 | 4,000 | 145 | 29 | 20.0 | 18 | 12.4 | 11 | 7.6 | Untrained subjects pressure breathing 8" of $H_2O$ |
| | (b) | 38,000 | 2.0 | 4,000 | 43 | 5 | 11.6 | 3 | 7.0 | 2 | 4.6 | Trained subjects pressure breathing 8" of $H_2O$ |
| 42 | (a) | 38,000 | 2.0 | 5,000 | 69 | 11 | 15.9 | 10 | 14.5 | 1 | 1.4 | Control diet + exercise 1st series (untrained) cont. oxygen |

## TABLE XXV (Continued)

| Reference | Altitude (ft.) | Time at altitude (hr.) | Average rate of ascent (ft./min.) | No. of man-tests | Total abdominal symptoms | | Abdominal symptoms no descent | | Abdominal symptoms with descent | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | No. | % | No. | % | No. | % | |
| (b) | 38,000 | 2.0 | 5,000 | 80 | 14 | 17.5 | 12 | 15.0 | 2 | 2.5 | Control diet + exercise 2d series (trained) |
| (c) | 38,000 | 2.0 | 5,000 | 69 | 7 | 10.1 | 7 | 10.1 | 0 | 0 | Control diet + exercise 3d series (trained) |
| Randolph Field data (a) | 38,000 | 2-3 | 3-4,000 | 1,729 | 542 | 31.3 | 457 | 26.4 | 85 | 4.9 | Untrained subjects demand $O_2$ |
| (b) | 38,000 | 2.0 | 4,000 | 192 | 30 | 15.6 | 27 | 14.1 | 3 | 1.5 | Trained crewmen demand $O_2$ |

## TABLE XXVI

*Miscellaneous factors present before ascent given by subjects as cause for abdominal symptoms at 38,000 feet (Randolph Field data)*

| | No. | Total abdominal symptoms | | Abdominal symptoms no descent | | Abdominal symptoms with descent | |
|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % |
| Chronic G. I. factors | | | | | | | |
| (a) Constipation | 26 | 21 | 80.7 | 12 | 46 | 9 | 34.7 |
| (b) Hernia present | 1 | 1 | 100 | 0 | 0 | 1 | 100 |
| (c) History of ruptured appendix | 1 | 1 | 100 | 0 | 0 | 1 | 100 |
| Acute G.I. factors | | | | | | | |
| (a) Cathartics | 3 | 2 | 66 | 1 | 33 | 1 | 33 |
| (b) Diarrhea | 4 | 3 | 75 | 0 | 0 | 3 | 75 |
| (c) Stomach-ache | 8 | 6 | 75 | 1 | 12.5 | 5 | 62.5 |
| (d) Eaten excess | 22 | 15 | 68.1 | 7 | 31.8 | 8 | 36.3 |
| (e) Missed meal before | 39 | 7 | 18 | 5 | 12.8 | 2 | 5.2 |
| Acute food factors | | | | | | | |
| (a) Rich cake | 1 | 1 | 100 | 0 | 0 | 1 | 100 |
| (b) Beans | 7 | 7 | 100 | 5 | 71.4 | 2 | 28.6 |
| (c) Milk in excess | 1 | 1 | 100 | 0 | 0 | 1 | 100 |
| (d) Sausage | 2 | 2 | 100 | 1 | 50 | 1 | 50 |
| (e) Bananas in excess | 2 | 2 | 100 | 2 | 100 | 0 | 0 |
| "Head colds" | 147 | 71 | 48.3 | 20 | 13.6 | 51 | 34.7 |

Taylor and Robinson (234) reported a case of functional cardiospasm which repeatedly caused symptoms at 38,000 feet. The distention was severe enough to reduce vital capacity 62%. After insertion of a stomach tube with expulsion of gas, the subject's vital capacity was 92% of normal. Collins (56) reported that a patient, age 23, with a congenital megacolon, first noted symptoms at 10,000 feet and complained of considerable abdominal distention, dyspnea, and precordial pain at 14,000 feet on an airplane trip. Symptoms disappeared when the plane lowered its altitude and reappeared on ascent to 14,000 feet. This time, however, he relieved himself considerably by passing gas. That altered anatomy and physiology are important is emphasized by this observation:

Colostomy patients are given an extra supply of clean bandag when evacuated by air, since gas and fecal material are discharged in excess from the orifice at altitude as compared to the rate at ground level. This is probably due to stimulation of colon motility by expansion of gas in the gastrointestinal tract and, of course, the absence of functional sphincters. Heath (123) reported a subject who had recurrence of abdominal pain on repeated ascents in the altitude chamber. Investigation showed a diaphragmatic hernia to be present.

*Acute or Chronic Gastrointestinal Upsets.* Temporary or prolonged deviations from the normal physiology of the gastrointestinal tract are attended by a high incidence of abdominal symptoms, many severe enough to cause descent. Chronic constipation, acute diarrhea, cathartics, etc., as possible causes of symptoms, are listed in table XXVI. In this series, "missing the meal before ascent" did not increase symptoms, although one report (230) indicates that discomfort occurred in a few individuals who had not eaten breakfast.

**Discussion.** As Gray (103) has pointed out, there are at least four factors concerned in the production of abdominal symptoms at altitude: (1) the quantity of gas in the bowel at sea level; (2) the amount of expansion at altitude; (3) the ability of the bowel to eliminate the expanding gas; and (4) the sensitivity of the bowel to pain. The relative and absolute importance of these several factors may vary widely within and among individuals so that one should be cautious in overstressing any one of them at the expense of the others.

*Quantity.* According to Blair et al. (33), the gastrointestinal tract of young men on a normal mixed diet contains approximately 1,000 cc. of gas. Most of the gas is found in the stomach and colon.

*Sources.* There are three sources of intestinal gas: (1) According to current opinion (179), most of the gas originates from swallowed air which is ingested with, or independently of, food

and fluids. Thus, we would expect the quantity of gas present to depend primarily on the degree of aerophagia. Apprehension and anxiety are factors which may increase this phenomenon (7, 179). (2) A second, and usually less important, source of intestinal gas is the putrefaction of food residues by bacterial action, primarily in the proximal colon. This factor might be expected to be influenced considerably by diet and by gastrointestinal stasis. In this connection, it is of interest to note that Kantor and Marks (153) cite a patient whose bowel produced so much hydrogen sulfide that silver sulfide was produced on the coins in his pocket. (3) A third source of intestinal gas is the blood stream. There is evidence that, given sufficient time, gases in the subcutaneous tissues (46), or in various body cavities—pleural (237), peritoneal (46), intestinal lumen (9, 178, 201)—tend to come into approximate tension equilibrium with the gases in venous blood. Gases will diffuse in one direction or the other, depending on the pressure gradient, until approximate equilibrium is reached. It may also be important in the "sudden bloating" which occurs in allergic individuals on eating certain foods.

*Composition.* Data on the composition of intestinal gas in normal human beings are meager, but that which is available confirms the expectation that most of the gas present is nitrogen (table XXVII) (9, 20, 81, 206). Smaller amounts of $CO_2$ and $O_2$ are present and, depending on the diet, a variable proportion of the putrefactive gases, $CH_4$, $H_2$, and $H_2S$ may be present.

To summarize a long discussion presented elsewhere (5):

Most of the gas in the intestinal tract at sea level is nitrogen.

On ascent to altitude, the intestinal gases expand according to Boyle's law, the major contribution to the expansion being nitrogen.

Diffusion of $O_2$, $CO_2$, and $H_2O$ from the blood is a potential source of additional gas expansion, at least during the first 30 to 60 minutes at altitude. Nitrogen diffusion cannot contribute very much to the total.

## TABLE XXVII

*Table showing marked variations in composition of colonic gases in man*

| | $O_2$ | $CO_2$ | $N_2$ | $CH_4$ | $H_2$ | $H_2S$ | Volume (cc./24 hr.) |
|---|---|---|---|---|---|---|---|
| Ref. 206 | | | | | | | |
| a. Milk diet 1 | — | 16.8 | 38.4 | 0.9 | 43.9 | | — |
| Milk diet 2 | — | 9.0 | 36.7 | 0 | 54.8 | | — |
| b. Meat diet after 24 hr. | — | 13.6 | 46.0 | 37.4 | 3.0 | | — |
| Meat diet after 48 hr. | — | 12.5 | 57.9 | 27.6 | 2.1 | | — |
| Meat diet after 72 hr. | — | 8.5 | 64.4 | 26.5 | 0.7 | | — |
| c. Diet of legumes 1 | — | 34.0 | 19.1 | 44.6 | 2.3 | | — |
| Diet of legumes 2 | — | 38.4 | 10.7 | 49.4 | 1.6 | | — |
| Diet of legumes 3 | — | 21.0 | 18.9 | 55.9 | 4.0 | | — |
| Ref. 81 | 0.7 | 10.3 | 59.4 | 29.6 | — | | 1,000 |
| Ref. 20 | | | Undetermined | | | | |
| Subject 1 | 8.8 | 10.3 | 80.9 | | | | 590 |
| Subject 2 | 7.9 | 4.9 | 87.2 | | | | 585 |
| Subject 3 | 9.2 | 2.5 | 88.3 | | | | 425 |
| Subject 4 | 11.4 | 2.6 | 86.0 | | | | 655 |
| Average | 9.3 | 5.1 | 85.6 | | | | |
| Ref. 9 (normal flatus) | | | | | | | |
| Subject 1 | 0.3 | 8.0 | 86.4 | 0.1 | 5.2 | 0 | |
| Subject 2 | 0.2 | 10.7 | 82.5 | 2.0 | 4.6 | 0 | |
| Subject 3 | 1.4 | 10.9 | 77.1 | 0.7 | 9.9 | 0 | |
| Subject 4 | 1.0 | 9.3 | 83.7 | 0.2 | 5.8 | 0 | |
| Subject 5 | 4.3 | 7.3 | 84.0 | 0.2 | 4.2 | 0 | |
| Subject 6 | 0.0 | 12.7 | 84.9 | 2.0 | 2.4 | 0 | |

Since, in high altitude exposures, most abdominal distress occurs either during ascent or within the first 5 minutes at peak altitude, and since, according to the above calculations, the diffusion of blood gases into the intestinal tract lumen requires

considerable time to reach completion, it is probable that the expansion of the original gas present, chiefly nitrogen, is mainly responsible for the production of abdominal symptoms at altitude. This does not mean that diffusion does not contribute; it undoubtedly does, and its contribution may be considerable. To evaluate its magnitude, experimental studies on closed loops of bowel would be of great interest.

Since conditions favor a tremendous expansion of intestinal gases during the first 30 to 60 minutes at altitude, absorption not being possible before this time, it is obvious that the expanding gas must be eliminated to prevent the occurrence of symptoms in most individuals.

It is pertinent in this connection to inquire into the theoretic value of denitrogenation in preventing abdominal distress at altitude. From theoretic considerations (5), we would expect that a maximum of only 30% of the nitrogen present in the bowel could be removed by breathing 100% oxygen at sea level for 1 hour, a procedure which is quite effective in reducing the incidence of "bends." There is considerable experimental evidence that such a procedure is actually quite ineffective in promoting the absorption of nitrogen from closed loops of bowel. Thus, in cats, McIver et al. (178) found no absorption of nitrogen from a closed loop of small intestine after 1 hour of oxygen inhalation and only 14% absorption after 2 hours. Fine et al. (77) placed nitrogen in closed loops of the small intestine in cats and found only 26.2% absorbed after 6 hours of oxygen inhalation and only 44.9% after 12 hours. Thus, one cannot expect much from relatively short periods of denitrogenation in reducing the original quantity of nitrogen present in the gastrointestinal tract. This procedure would, of course, have no effect on the expansion of gases due to the diffusion of $O_2$, $CO_2$, and $H_2O$ from the blood. It would reduce the diffusion of nitrogen, but this is an insignificant factor.

The sensitivity of the bowel to pain and the elimination of the expanding gas in the bowel at altitude are important factors. It is instructive to consider briefly the resistance offered by the bowel when gas expands. There is a resistance which depends

upon the elastic characteristics of the colon wall and the motility and tone of its musculature. This resistance will reduce the actual expansion of the gases below the theoretic values which can be calculated, and any such reduction will be accompanied by a corresponding rise in the intraluminal pressure. The question then arises as to how much distention or how great an increase in intraluminal pressure is necessary to produce symptoms. The available data indicate that the potential expansion of intestinal gases at 38,000 feet and even lower is adequate to produce not only mild symptoms, but also rather severe symptoms in some individuals (205).

Thus, 14 to 26 cc. of air (measured at room temperature and ambient pressure) introduced into a balloon in the lower esophagus will produce a burning distress (191). The corresponding intraluminal pressure varied from 80 to 150 mm. Hg. According to Chapman and Jones (53), an intraluminal pressure of 27 mm. Hg will produce pain in the lower esophagus.

In the stomach (191), 400 to 500 cc. of air will usually produce symptoms which are variously described as "fullness," "sickish gas pain," "ache," "cramps," "bloating," etc. In these experiments, intraluminal pressure rose rapidly to about 40 mm. Hg with the introduction of the first portion of air, but then remained relatively constant when more was added.

In the duodenum, Ivy (140) found that 50 cc. of air would produce nausea and chilliness. According to Polland and Bloomfield (191), 50 to 100 cc. of air introduced into the duodenum are usually adequate to produce symptoms variously reported as "severe sharp pain or ache," "hot sticking pain," or "burning cramp." Nausea and vomiting occurred frequently. Intraluminal pressures of 60 to 120 mm. Hg were recorded.

Forty cc. of air introduced into the jejunum will produce pain, according to Jones (146).

In the descending colon (191), it was found that 100 to 200 cc. of air introduced into a balloon was usually adequate to produce

symptoms described as "severe cramping pain," "gas pain," "gassy distended feeling," "awful stomach-ache," etc. Intraluminal pressures were not reported.

It would, thus, appear that a volume of gas in the neighborhood of 100 cc. confined in a localized segment of the duodenum, jejunum, or colon is adequate to produce symptoms. Considerably less than this is adequate in the esophagus, and considerably more is necessary in the stomach. According to previous calculations (5), such volumes should be easily attained by the expansion of intestinal gases on ascent to altitude.

The facility with which the expanding gases at altitude are eliminated, or the degree of abdominal distress when the gases are not eliminated, may depend upon the motility of the gastrointestinal tract.

### *Motility of Bowel and Elimination of Expanding Gas at Altitude*

#### General concepts of motility

We may use the colon as an example of an organ concerned in production of abdominal symptoms. The motility of the alimentary tract may be classified primarily as propulsive or nonpropulsive.

Propulsive motility constitutes about 10% of the total motility (2) and, by definition, implies that intersegmental motility is synergized or coordinated and that the contents of the bowel are moved.

Normally, about 90% of the colon motility is nonpropulsive, which means that, intersegmentally, the motility is relatively unorganized.

The colon is composed of functional segments which cannot be described on a structural basis. Anatomically, the segments are referred to as ascending, transverse, and descending colon, but on the basis of motor activity, the colon is composed of small or large divisions depending upon the type of motility which is manifested

at any particular time. When two adjacent segments 5 cm. apart manifest the same general type of activity so that a propulsive wave passes from one to the other, then the two segments represent an integrated or coordinated functional unit 5 cm. in length. In a "mass peristalsis," as in defecation, an entire anatomic division of the colon may represent a functional unit which is 50 cm. in length.

### Dyskinetic motility induced by expansion of gas

Normally, one is not conscious of a propulsive wave in the colon. However, when a strong propulsive wave occurs in a proximal segment of the bowel and is not "accepted" by the distal segment because of the latter's dyskinesia or incoordination, a sensation of tension bordering on a cramp may be experienced. Gas, in particular, when acted upon by strong motility, tends to cause these symptoms and is often difficult to propel. It is even possible that gas can be moved proximal to its original location instead of distal as might occur if a strong propulsive wave should encounter a dyskinetic distal segment with high tonus. Under these conditions, the strong motility increases the intraluminal pressure momentarily in local areas as the wave progresses. When the functionally obstructed area is encountered, the gas under increased pressure will tend to return proximally to areas of reduced pressure.

Dyskinetic motility per se can be a cause of intestinal pain independent of the quantity of gas present in the gastrointestinal tract. This fact was noted in studies of colostomy patients which extended over a period of a year (2, 3). In this connection, Templeton (236) noted gastric pain in some subjects with no x-ray evidence of abnormalities in stomach motility.

It is possible that these strong colonic waves, which are not well integrated with distal segments, operate to produce some of the symptoms of gaseous distention at high altitude. It is more logical to believe that if strong intestinal waves were exerting force against a large quantity of gas, abdominal symptoms would be experienced to various degrees depending upon practically all

the factors enumerated in this paper. It should also be pointed out that inhibition or relaxation of some segments of the colon to an excessive degree and for long periods of time is just as much a part of the concept of colon dyskinesia as is high tonus, spasm, or dyskinetic motility. Such "ballooning out" of some segments with motility in others has been noted to occur not only after administration of morphine to human subjects (1), but also spontaneously (2). With these concepts in mind we may proceed to theoretic explanations of the mechanisms of certain instances of abdominal symptoms at high altitudes.

A common observation at altitude is that passage of gas as flatus or by eructation usually affords relief of abdominal symptoms which occurred on ascent or shortly after reaching altitude. In these instances we may assume that the initial symptoms were due to:

1. Gas expansion causing distention of the bowel. The most common and effective stimulus to gastrointestinal motility is a moderate degree of distention of the intestinal wall (48).

2. The propulsive motility initiated by such distention caused passage of gas which relieved the distention. This passage of gas probably was effected by propulsive motility, but passive overflow through cardiac and anal sphincters might also occur.

In a number of cases of abdominal pain at high altitude, large amounts of gas are expelled but only slight relief of pain is afforded. If we assume that the original volume of gas is reduced by expulsion of gas, then it may be true that dyskinetic motility persists or that the residual gas is sufficient to distend an irritable focus, and dyskinetic motility exacerbates pain. It may also be possible that the gas which is passed is replaced by gas from more proximal segments or, if sufficient time elapses, by gas from the blood; hence, in spite of gas elimination, the resultant reductions in overall pressure and volume are insufficient to relieve symptoms.

Abdominal gas symptoms may disappear at altitude without perceptible eructation or passage of flatus. It is possible that:

1. The quantity of gas was decreased by imperceptible passage of flatus or eructation. Normally 380 to 655 cc. of gas can be collected in 24 hours from individuals unaware of its passage (20).

2. The bowel adapted itself to the stimulus caused by gas expansion by moving the gas to less irritable foci.

3. Dyskinetic motility stimulated by distention ceased.

4. If the elapsed time at altitude were great enough, considerable gas may be absorbed from the bowel into the blood and eliminated through the lungs. It is of interest to note that, at a Subcommittee Meeting on Intestinal Gas (179), it was postulated that the swallowing of air might contribute not only to bowel disturbance, but also, through its absorption at altitude, to production of aero-embolism.

In a few but definite instances, abdominal symptoms severe enough to cause descent were noted to begin in the latter part of a 2- or 3-hour exposure to 38,000 feet. Theoretically, this might occur if:

1. Enough oxygen were swallowed to cause distention.

2. Accumulation of gas occurred in local regions after expulsion from proximal regions of the bowel.

3. Dyskinetic motility appeared with relative suddenness. That this can occur has been shown previously (2).

Abdominal pains at altitude vary from mild to severe and may be sharp or dull; in addition, they may decrease in severity, attain a relatively steady state, or be progressive or intermittent. Occasionally, if severe, they may persist for 24 hours after descent (16). The concept of gastrointestinal dyskinesia may be used to explain these phenomena. For example, intermittent distention symptoms were noted to occur in colostomy patients concomitantly with motility and tonus characteristically dyskinetic in nature. At unpredictable moments the motility would become intersegmentally synergized, colon contents would be moved, and immediate alleviation of symptoms result (2). It is possible that intermittent abdominal distress at altitude is due to such a mechanism. Unfortunately, x-ray data is incomplete on this point and probably would fail to be conclusive because interpretation is difficult without extensive knowledge of normal motility patterns for each subject. Unfortunately, also, as far as the x-ray interpretation is concerned, the facts are:

1. If some of the gas is passed, the pressure or tension is reduced and, hence, symptoms due to distention may be lessened.

2. The remainder of the gas, however, may expand volumetrically and occupy almost as large an area. Because of technical factors, any changes in density of gas shadows in x-ray exposures before and after gas expulsion may be difficult to interpret. Thus, it might be assumed by x-ray that the same quantity of gas was present in an area when such was not the case The above factors may be the explanation for such statements as "there was no correlation between the amount of gas expelled to the changes in volume of the intestinal gas or relief of symptoms" (33).

### Dyskinetic motility due to psychic factors

There are no controlled altitude experiments specifically dealing with the relation of preflight psychic factors to the incidence of gas pains. McLester (179) gave anxiety as a factor, and Blair et al. (33) have indicated in x-ray studies that the quantity of intestinal gas may be increased by anxiety.

Other evidence that psychic factors may play even a minor role in the occurrence of abdominal distress at altitude must necessarily be shown indirectly. This can be done by correlating clinical concepts of the etiology of gastrointestinal symptoms with the type of abdominal symptoms encountered in high altitude studies.

Many types of clinical evidence exist which show that rapid changes of motility and gas content of the gastrointestinal tract with production of symptoms take place under conditions of anxiety and apprehension. A few examples should suffice:

1. The chronic "belcher" is often a neurotic who, with a few swallows of liquid, can also ingest 500 cc. of air. This air usually reaches only the lower esophagus and produces symptoms of fullness and bloating, but may reach the stomach (7).

2. A peculiar type of powerful sighing respiration can soon fill the stomach with air (8). Possibly this is a factor on ascent to altitude when oxygen masks are put on for the first time and a degree of anxiety is present in some individuals. In this connection, Behnke and Willmon (30) found that the use of a mouthpiece for helium-oxygen respiration led to large quantities

of gas being swallowed with production of subsequent severe abdominal symptoms. In fact, masks had to be substituted. They also strictly limit the chewing of gum before ascent to altitude for the same reason.

3. Warren, quoted by Alvarez (8), had noted that "the first film made by a sensitive patient just before he submits to the passage of ureteral catheters usually shows but little gas, whereas the second film made after the catheters are in place shows the small bowel to be filled with gas." Presumably, some of the gas in the intestine is apparently excreted from the blood because of change in vessel permeabilities caused by blanching and blushing of the mucosal vessels brought on reflexly.

4. Practically all altitude chamber tests are conducted on relatively young male adults in good health. It may, however, be safely assumed that there is a certain amount of preflight tension even in veterans of many exposures, but especially in novices. In the latter group, one could expect to find a small group of susceptible individuals who, when put under strain, have gastrointestinal symptoms as part of their total response. These occur even at ground level. Obviously, ascent to altitude with its resulting gas expansions should, in some cases, aggravate the condition for the following reasons: (a) The stomach and colon of men are easily influenced reflexly by anxiety and apprehension through extrinsic nervous pathways. It is well known that altered motility of these organs result. (b) Since the *quantity of gas* is an important factor in production of symptoms, added to the anxiety effect, most of the free gas which could be expected to expand with decreased barometric pressures is found to be situated in the stomach and colon. Summation of factors (a) and (b): Varying degrees of these two factors could result in symptoms of distention which would be dependent upon the extent to which the altered gastric and colonic motility initiated by anxiety was unable to move trapped gas.

5. Distention of the gastrointestinal tract is the most efficient stimulus causing changes in tonus and motility. Some changes are local to the area of distention. Some changes occur in other portions of the tract by entero-enteral reflexes. The degree of pain, distention, bloating, etc., caused by these changes is also dependent upon a number of factors: (a) The colon usually has a higher threshold for pain caused by distention than the small intestine of the normal subject. (b) There is a wide variation in the threshold for intestinal pain among various subjects. This is usually explained clinically by considering that only in some people does the gastrointestinal tract act as a "sounding board" for reflex nervous symptoms. Stated another way, the stomach and colon of some individuals are more "educated" to functional dyskinesia and the threshold for pain is not so high. That the gastrointestinal tract may be "educated" to pain is supported by this type of evidence. Subjects have swallowed balloons which were distended to cause pain. Early in such studies localization is poor, and generalized

discomfort occurs much as in abdominal symptoms at altitude. After several tests, however, the subject can localize his symptoms to more definite areas. Many such experiments checked by x-ray have been performed by Ivy (140).

## Effects on the Ear

One of the most common manifestations of altitude dysbarism is the effect of barometric pressure changes on the middle ear. The importance of these effects in aviation medicine have been discussed by Armstrong (15-17). In caisson disease, the data of Heller et al., quoted by Hill (129), showed that ear difficulties constituted about 21.5% of the total symptoms.

Initial symptoms arise as a result of poor ventilation of the middle ear due to inadequate function of the eustachian tube during changes in barometric pressure. Repeated episodes of barotraumatic injury to the tympanum may result in chronic as well as acute effects.

### Definitions

*Barotalgia.* Ear pain caused by dysbarism of the middle ear. Barotalgia refers to the *acute* barotraumatic injury producing varying degrees of fullness and pain.

*Barotitis Media.* An *acute* or *chronic* traumatic inflammation of the middle ear caused by dysbarism. It is acute when infection or inflammation of the middle ear follows dysbarism within hours or a few days. It is chronic in those individuals who have had repeated barotraumatic injury with repeated otitis media.

*Barotitis Externa.* An *acute* or *chronic*, traumatic ear condition resulting in inflammation of the external auditory canal and tympanic membrane and caused by a pressure differential between the external auditory canal and the middle ear, usually associated with complete plugging of the external ear.

*Barotraumatic Deafness.* An impairment of hearing, usually temporary, which is part of the syndrome resulting from barotraumatic injury to the ear. Barotalgia and barotitis media are especially prone to cause temporary losses of hearing and it seems likely that permanent impairment of varying degree may result from repeated episodes.

### Physiologic mechanism of otic barotrauma

The physiologic mechanism is that of a failure to equalize pressure on the two sides of the tympanic membrane during changes in barometric pressure. This failure in pressure equalization arises chiefly as a result of the peculiar structure and inadequate function of the flutter-valve-like orifice of the eustachian tube.

Normally, the pharyngeal valve of the eustachian tube favors the movement of air from the middle ear to the nasopharynx and opposes the passage of air from the nasopharynx to the middle ear. Several situations of interest can be schematically diagramed as follows:

*Normal Sea Level Conditions.* At sea level, the pressure on both sides of the tympanum is 760 mm. Hg (fig. 1).

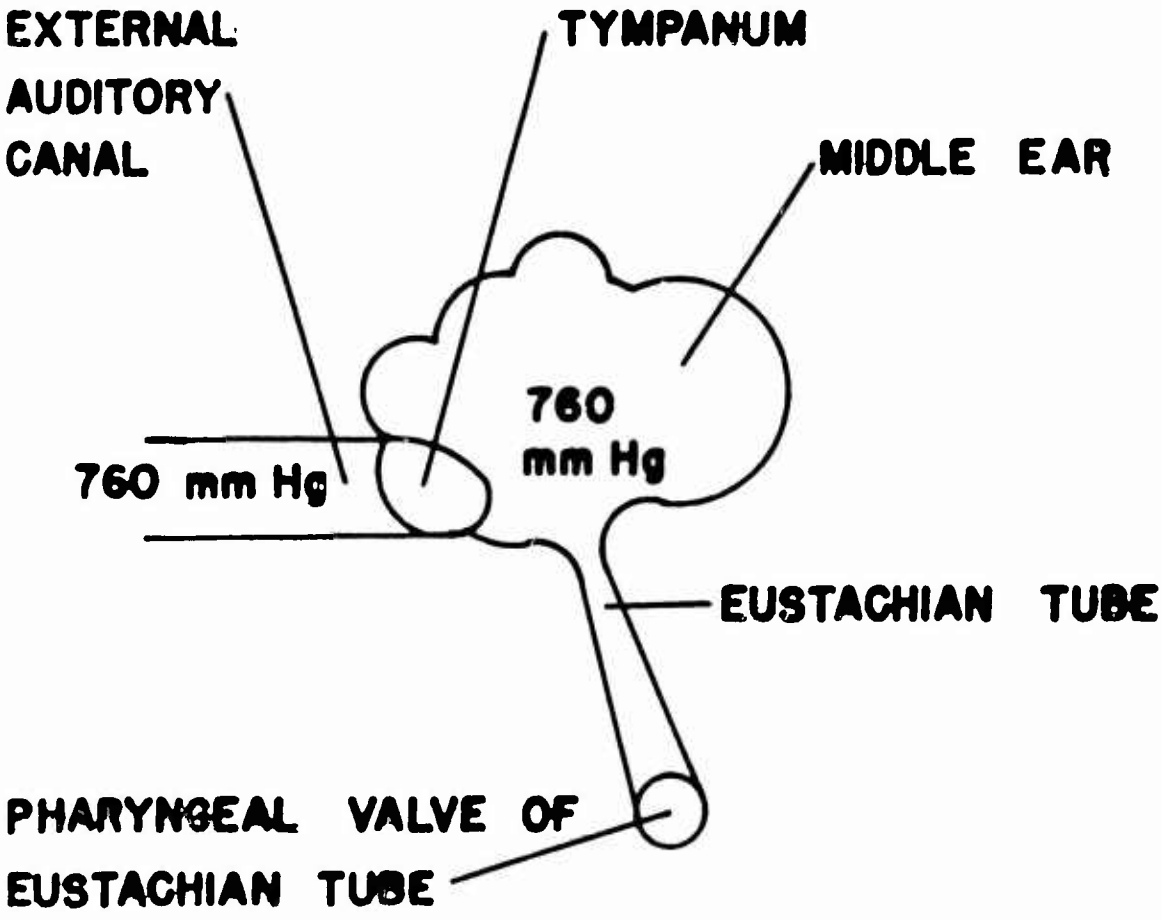


FIGURE 1
*Normal sea level conditions.*

Armstrong and Heim (17) have recorded quantitative data on differential pressures as they affect the equalization mechanisms and cause ear symptoms.

Beginning at sea level pressure and on *ascent* to altitude, a differential pressure of only 3 to 5 mm. Hg was needed before there was a slight sensation of fullness in the ears. Examination showed a slight *bulging* of the tympanum until at a 15 mm. Hg differential there was a sudden "click" which was heard and felt in the ear. With this "click" the eardrum no longer bulged, which meant that the eustachian tube valve had been forced open by the expanding air in the middle ear. As ascent was made, values other than 15 mm. Hg were recorded in the same individual. The differential pressure needed to "force" the eustachian valve on ascent from sea level varied from 5 to 30 mm. Hg in different individuals, but the average values for the same individual were remarkably constant.

*Obstruction of Eustachian Tube.* Acute or chronic conditions such as upper respiratory infection, inflammation of the eustachian tube, tumors, malposition of the jaws, or hypertrophy of the adenoid tissue (Gerlach's or tubal tonsil) at the orifice of the eustachian tube can cause inadequate function of the valve either on ascent or descent.

## Ascent to 5,000 feet

If ascent were made to 5,000 feet (632.4 mm. Hg) and the eustachian orifice were completely blocked, then the differential pressure across the tympanum would be 760 — 632.4 = 127.6 mm. Hg (fig. 2). The tympanum would offer resistance but would be *bulged outward.* In some individuals, the tympanum might possibly rupture since a differential pressure between 100 to 500 mm. Hg can cause rupture (17). Behnke (23) gives the values at between 250 to 500 mm. Hg.

Instances of severe otic barotrauma *on ascent* are not nearly as frequent as those on descent and this is understandable since the eustachian valve favors movement of air out of the eustachian tube

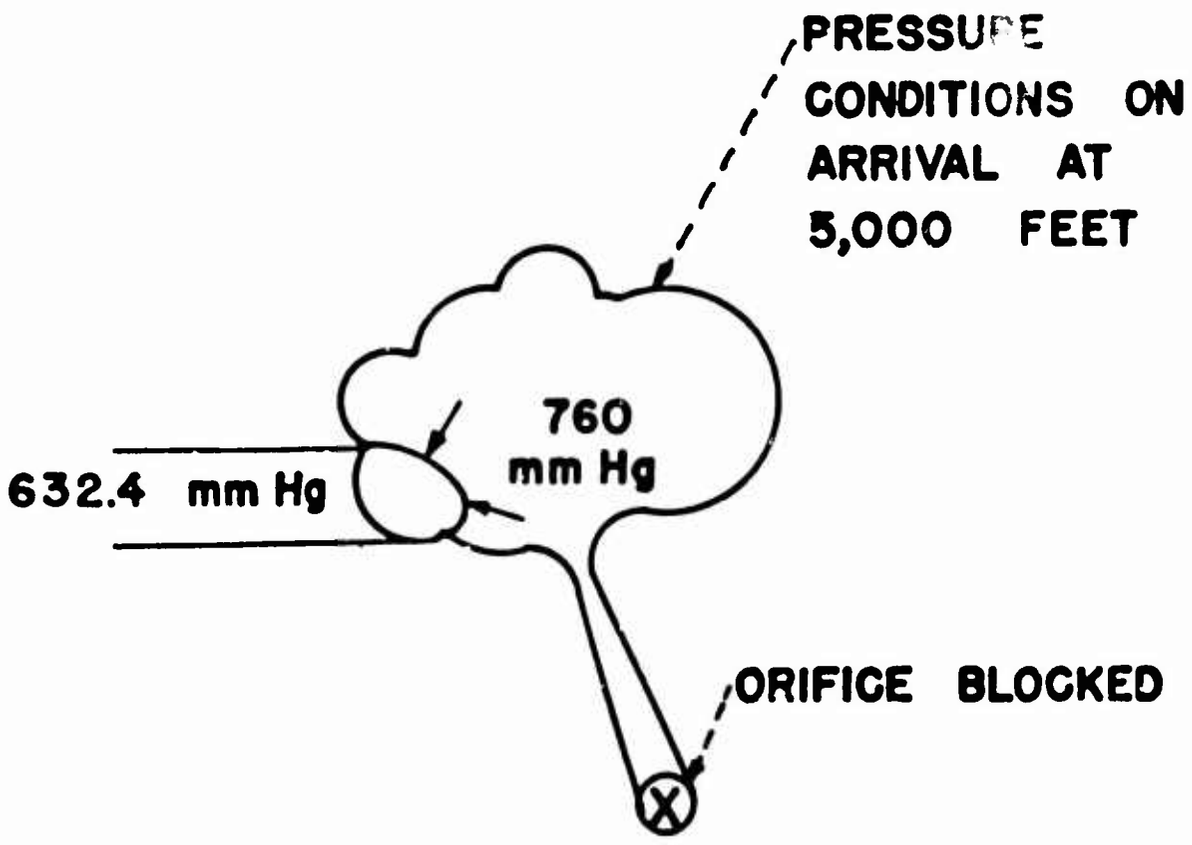


FIGURE 2

*Ascent to 5,000 feet.*

so that normally, at 5,000 feet, the pressure on both sides of the tympanum would be in the neighborhood of 632.4. mm. Hg.

## Descent from 5,000 feet

Suppose that an individual at 5,000 feet had equal pressures on both sides of the tympanum (632.4 mm. Hg). If the eustachian orifice was completely blocked and this individual was returned to sea level, then the pressure differential across the tympanum would again be about 127.6 mm. Hg, but the membrane would be retracted—that is, pushed in—by the excess pressure in the external auditory canal (fig. 3).

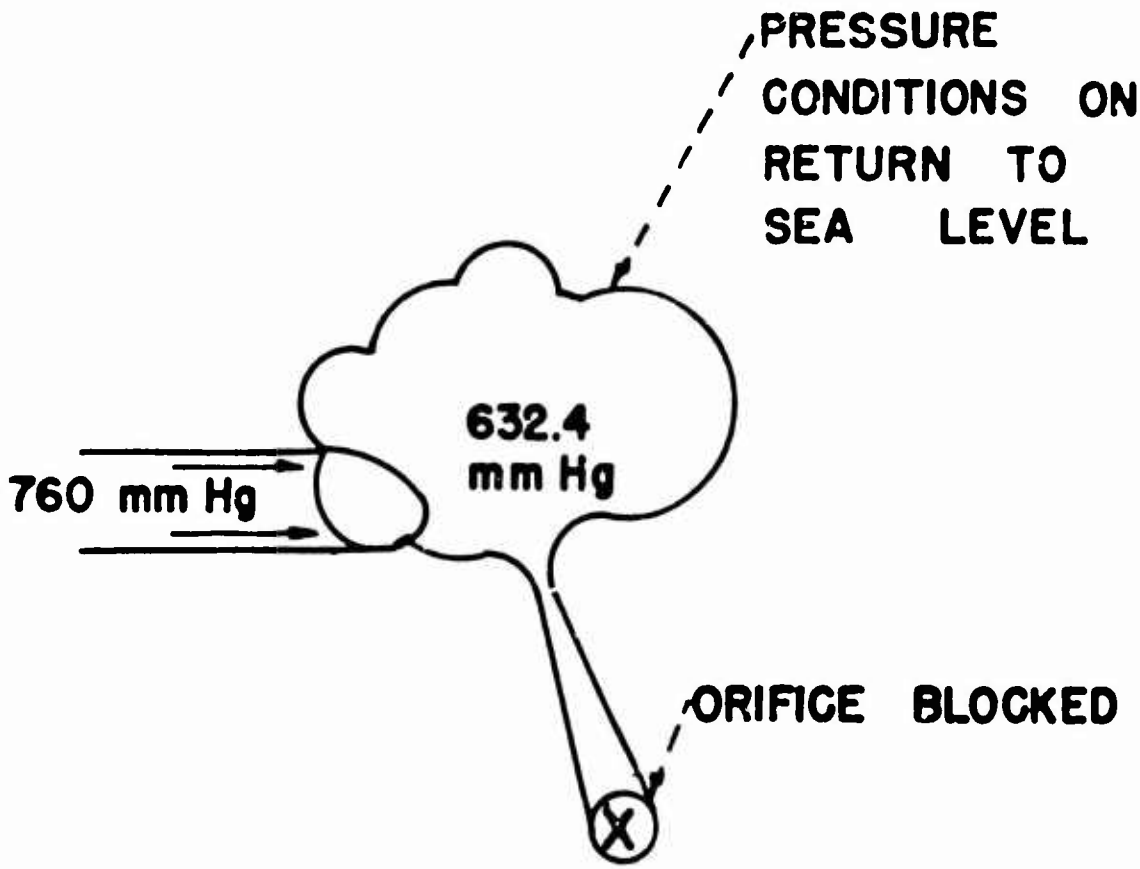


FIGURE 3

*Descent from 5,000 feet.*

Instances of otic barotrauma are most frequent on *descent* because the flutter-valve-like action of the eustachian tube valve opposes passage of air from the nasopharynx into the eustachian tube and middle ear.

The eustachian valve normally opposes the passage of air from the nasopharynx into the middle ear. This causes the greatest disadvantage to the caisson worker and diver because, on being exposed to pressures greater than atmospheric, the only way the pressures in the external auditory canal and the middle ear can be equalized is by forcing the eustachian valve to pass air from the nasopharynx into the middle ear. In addition, the barotraumatic injuries to the ear of the diver or caisson worker may be more severe as well as more frequent because of the greater ranges in pressures to which such individuals are exposed. For

example, if the diver is exposed to 2 atmospheres of pressure (2 × 760 = 1,520 mm. Hg), and if the eustachian valve is completely closed, he will have 1,520 mm. Hg pressure in the external auditory canal and only 760 mm. Hg pressure in the middle ear. Such a differential pressure of 760 mm. Hg would most likely rupture the eardrums.

The functional inadequacy of the eustachian valve is chiefly responsible for dysbaric symptoms of the middle ear. One should keep in mind, however, that congenital malformations, tumors, infections, etc., of the *external auditory canal* could also cause some opposition to the free passage of air in and out of the canal and result in dysbarism of the middle ear. If the external auditory canal were completely obstructed in a region external to the tympanum, then on ascent the air between the obstruction and the tympanum would expand and push the eardrum in, provided the expanding gas in the middle ear escaped from the eustachian tube. Other situations and combinations of factors could be elucidated, but the incidence of such cases is small.

Voluntary maneuvers to equalize the pressure on the two sides of the tympanum are usually successful, especially on ascent. It is necessary, however, to point out one aspect of pressure equalization difficulties; that is, *when the pressure is lower in the middle ear than in the external auditory canal* as occurs on descent from altitude or compression of a diver. If, on descent from altitude, air does not freely enter the nasopharyngeal valve of the eustachian tube to balance the increasing pressure in the external auditory canal, then the pressure in the middle ear is "relatively negative" as compared to the pressure in the external auditory canal. When a "negative pressure" of from 80 to 90 mm. Hg is developed in the middle ear, then the fibrocartilaginous portion of the eustachian tube is collapsed and the two chief muscles (tensor veli palatini—tenses the soft palate and opens the eustachian tube; salpingopharyngeus—raises the upper and lateral parts of the pharynx and opens the ostium of the eustachian tube) cannot overcome negative pressures of this magnitude (17). In other words, such voluntary efforts as swallowing and yawning are inadequate to open the eustachian tube and *ascent* to lower pressure should be made to decrease the magnitude of the differential pressure.

Of lesser significance is the phenomenon which sometimes occurs when individuals have been breathing supplementary oxygen at altitude and then return to sea level pressure. It is thought in this instance that the gas in the middle ear is chiefly oxygen, and when this oxygen is absorbed into the blood there may be a slightly negative pressure developed in the middle ear (16), accompanied by a feeling of fullness and "gurgling" sensations if fluid is present. These symptoms may occur from 2 to 6 hours after a flight and endure for a variable length of time. The usual experience is a sudden "snapping" sound which is felt and heard in the ear and most likely indicates the return of the tympanum to its normal position when the negative pressure in the middle ear is suddenly equalized by air entering through the eustachian valve. Concomitantly with the equalization of pressure, the feeling of fullness disappears and hearing is improved, provided the barotrauma has not been severe. Possibly, the above phenomenon could be experienced by patients breathing oxygen at ground level.

Tables XXVIII and XXIX have been tabulated from Armstrong and Heim (17).

## TABLE XXVIII

*Pressure in the middle ear is greater than in the external auditory canal (17)*

| Pressure higher in middle ear (mm. Hg) | Symptomatology |
|---|---|
| Plus 3 - 5 | Perceptible feeling of fullness in the ear. |
| Plus 10 - 15 | Distinct feeling of fullness. Lessened sound intensity. |
| Plus 15 - 30 | Increased discomfort with tinnitus of a hissing, roaring, crackling, or snapping character. May be pain and mild vertigo. (Pressure of 15 mm. Hg is normally sufficient to force the eustachian valve and equalize the pressure—produces an annoying "click" which is heard and felt in the ear.) |
| Plus 30 or more | Increasing pain, tinnitus, and vertigo. |

## TABLE XXIX

*Pressure in the middle ear is less than in the external auditory canal (17)*

| Pressure lower in middle ear (mm. Hg) | Symptomatology |
|---|---|
| Minus 3 - 5<br>Minus 10 - 15<br>Minus 15 - 30 | Same as listed in table XXVIII. |
| Minus 60 | Severe ear pain, marked tinnitus, vertigo, and beginning nausea. |
| Minus 60 - 80 | Severe ear pain radiates to temporal region, parotid gland, and the cheek; deafness is marked; vertigo and tinnitus usually increase but tinnitus may disappear. |
| Minus 100 - 500 | Tympanic membrane ruptures. |

The following is quoted directly because of its descriptive excellence (17):

> At between 100 and 500 mm. of Hg (differential pressure between the middle ear and external auditory canal) the tympanic membrane ruptures.
>
> This occurrence is a dramatic episode in which the patient feels as though hit along the side of the head with a plank. A loud explosive report is felt and heard in the affected ear, there is a sharp piercing pain on the affected side, vertigo and nausea become marked and collapse or generalized shock follows. With rupture of the tympanic membrane the acute pain quickly subsides, but a dull ache persists for from twelve to forty-eight hours. Hearing is distinctly diminished and vertigo and nausea may persist for from six to twenty-four hours.

The incidence of barotalgia is affected a great deal by the speed of descent and the season of the year. It should be sufficient to mention here that when emergency rapid descents are effected with the low pressure chamber the incidence of ear pain is considerably increased, and when the seasonal increase of head colds occurs, more individuals have difficulty descending from altitude.

The monthly and annual reports of many altitude units indicate the overall incidence of barotalgia in many thousands of subjects

is 3 to 6%. The incidence of barotalgia resulting in complications such as infection or rupture of the eardrum is very small. In 2 months of operation, the 31st Altitude Training Unit reported 6 severe cases, an incidence of less than 0.3%.

### Barosinusitis

Barosinusitis associated with ascent to high altitude in either aircraft or the low pressure chamber is not a major source of difficulty. However, the pain is extremely distressing when it does occur. The incidence is highest on descent. A study of 2,351 individuals indoctrinated at an Altitude Training Unit revealed that sinus difficulties developed in 35, an incidence of 1.5%. The incidence in two other groups of 62,160 and 21,560 trainees was 1.1 and 1.52%, respectively (60).

Further physiologic aspects of barosinusitis are discussed in the section on barodontalgia and in School of Aviation Medicine Textbook No. 4, January 1950, entitled "Aviation Otolaryngology."

### Barosinusitis

Air in the mastoid cells would be subject to expansion and the creation of unequal pressures just as air in any other body cavity. Occasionally a subject has developed symptoms which could have been baromastoiditis. Probably, the incidence is somewhat higher than we think, but the condition has passed unnoticed or mistaken to be a referred barotalgia.

### Barodontalgia

Pain in the teeth due to changes in barometric pressure does not have a high incidence but is of significance. Fortunately, the condition is correctible.

**Incidence.** Table XXX shows that the incidence of barodontalgia is small. Two studies (199, 225), however, indicate that a high percentage of the cases which do occur have severe pain, which means that descent was probably a necessity. Of 53 man-

## TABLE XXX

*Barodontalgia*

| Reference | Total tests | Total incidence | | Severe tooth pain | | Comment |
|---|---|---|---|---|---|---|
| | | No. | % | No. | % | |
| 199 | 3,438 | 63 | 1.86 | — | — | |
| 199 | 920 | 37 | 4.02 | 32 | 76.2 | 37 individuals with 42 cases of toothache |
| 190 | 87 | 5 | 5.8 | — | — | Civilian subjects |
| 164 | 12,000 | 202 | 1.6 | — | — | Altitude training unit, Las Vegas, Nev. |
| 208 | 2,351 | 25 | 1.06 | — | — | |
| 210 | 36,712 | 524 | 1.40 | — | — | Altitude training unit, Santa Ana, Calif. |
| 225 | 7,000 | 112 | 1.6 | 56 | 50 | Approximate values |
| 151 | — | — | 1.2 | — | — | Altitude training unit, several thousand cases |
| 35 | 2,300 | 27 | 1.17 | — | — | USN Air Training Center, Pensacola, Fla. |
| 60 | 62,160 | 635 | 1.02 | — | — | Altitude training unit |
| 60 | 21,560 | 161 | 0.75 | — | — | Altitude training unit |
| Total | 148,528 | 1,790 | 1.2 | — | — | |

flights to altitude which had to be discontinued, 5 (9.4%) were due to barodontalgia without other symptoms of dysbarism (230). It is of interest that a small series of civilian subjects had a higher incidence of barodontalgia than did military groups (190). This was attributed to better dental care in the latter. Of 603 experienced fighter pilots, there were 79 (13.1%) who said that they had experienced barodontalgia at least once (92). This percentage is high as compared to chamber runs, but the survey encompassed the entire flying experience of each pilot, not one chamber run. The overall incidence of barodontalgia is about 1.2%.

**Altitude of onset.** The altitude at which barodontalgia begins has been variously estimated to be from 5,000 to 15,000 feet. Mitchell (180) reported a case which began at 8,000 feet and quotes

Dreftus (64) as reporting tooth pain at 6,100 feet. Reynolds et al. (199) found some cases to begin as low as 1,000 feet, but in most cases pain was reported at 17,000 to 19,000 feet. The figures reported by Brickman (35), however, show that there was no range of altitude at which the onset of dental pain occurs with greatest frequency. He had cases beginning at 5,000 feet and up to 40,000 feet. Joseph et al. (151) concluded that the onset of tooth pain had no particular relationship to a specific altitude except that the greatest number of pain reactions occurred at the higher altitudes; 57% of their cases had pain at 28,000 feet, 23% at 18,000 feet, and the remaining 20% at 10,000 feet or below. Most of the investigations cited show that pain in the majority of cases occurred during ascent and that when tooth pain was noted it disappeared promptly when descent was effected, often at approximately the same altitude at which the symptoms first appeared. In their series, however, Reynolds et al. (199) found that only 13.5% of their subjects experienced pain on ascent and 86.4% on descent. The determination that barodontalgia occurs on ascent or descent is important from the viewpoint of the etiologic mechanism which is considered later.

**Symptomatology.** Barodontalgic pain ranges from a dull ache to being sharp and severe. It can be persistent over a considerable pressure range or occur in brief flashes. The onset of pain may be sudden at any altitude or gradually build up as higher altitudes are attained. If the pain occurs on ascent or at the peak altitude, then descent usually brings relief. Conversely, if the pain begins on descent, then reascent is usually effective. In at least one instance, tooth pain was associated with symptoms of collapse (171). An analysis of 852 forced descents from 2,920 man-flights at 35,000 to 38,000 feet revealed that toothache was responsible for 10 (1.2%) of the descents.

**Etiology.** The etiologic mechanism of barodontalgia may not be as obvious as has been postulated in the past. When tooth pain occurs on ascent, and in some cases there are symptoms as low as 1,000 feet, it seems reasonable to suppose that the mechanism is expansion of trapped air in spaces underlying mechanically faulty fillings. There is hearsay evidence only that individuals

have lost fillings at high altitude presumably due to the pressure exerted by the expansion of trapped gas. McDowell (175) thought that the loss of defective fillings at high altitude was coincident with intense clenching and grinding of teeth during physical and emotional tension, and not necessarily due to gas expansion under a filling. Restarski exposed properly and improperly filled teeth imbedded in artificial stone to altitudes from 10,000 to 60,000 feet without displacement of any of the fillings (138). However, when he immersed all of the filled teeth in a staining solution and exposed them to altitude, he found that large amounts of the solution had entered those with air cavities. There was no perceptible stain in those properly filled. These results were interpreted as meaning that during rapid ascents and descents oral fluids could be forced under leaky fillings or ones with air spaces and thereby cause toothache.

As causes of tooth pain have appeared, they have been investigated. In individual cases, untreated caries, poorly filled teeth with air spaces, periapical abscesses, cysts, acute and subacute pulpitis, temperature, vibration, etc., have been given as an explanation for poor altitude tolerance. Attention has been called to the fact (199) that most of these factors can be ruled out; they were considered as factors by the various authors only because barodontalgia occurred, dental examination was made, and the conditions were found. The authors refute the idea that the dental condition necessarily explained the tooth pain. They selected 14 individuals with major dental pathology and showed that on exposure to altitude none of these individuals had tooth or sinus pain. It was true in their series as in others, however, that 94.5% of the individuals who had tooth pain at altitude also had significant dental pathology in the areas of pain. This suggested a possible mechanism.

In recent years there has been a tendency to emphasize the close relationship between barosinusitis and barodontalgia (35, 92, 151, 157, 199). Reynolds et al. (199) have made several correlations of this relationship. They point out that (1) most of their cases of barodontalgia occurred on descent which strongly relates the condition to maxillary sinusitis; (2) their incidence of tooth pain

on ascent was only 13.5%, but even this does not necessarily suggest a mechanism other than sinusitis, because their incidence of frontal sinus pain during the same period was 10.7% and they believe frontal sinus pain occurs on ascent as well as descent; (3) a fairly large number of cases of tooth pain (38.1%) were associated with maxillary sinus pain; (4) in 35 (94.5%) of their 37 cases of barodontalgia, the pain was located in particular teeth or in an area approximating the maxillary sinus; (5) 31 of their 37 cases (83.8%) were relieved of their barodontalgia either during the chamber run or immediately following by politzerization or the Valsalva maneuver. The other 6 subjects lost their tooth pain spontaneously.

To further elucidate the relationship of barodontalgia and barosinusitis, Hutchins and Reynolds (138) chose 14 patients with various dental conditions requiring treatment but with no history of sinusitis, etc. Their procedure was to correct the dental condition without anesthesia or to use general anesthesia for extractions. Approximately 1 week later the mucosa in the region of the maxillary sinus was stimulated by a needle prick. Painful symptoms were produced in the treated teeth in 92.8% of the cases. In those cases in which only 1 tooth was treated, pain was localized to the particular tooth in 78.5%. Another series (198) was carried out in which the teeth of the same 14 patients were anesthetized on the proper side. Stimulation of the maxillary sinus ostium ipsilaterally produced no pain on the anesthetized side. Stimulation of the contralateral sinus ostium produced tooth pain. The above effects could be shown to persist for several months. From these experiments and observations the authors hypothesized that the mechanism of barodontalgia was that of referred pain chiefly from the maxillary sinus. The pain was referred to teeth which showed evidence of previous painful stimulation as by filling, trauma, caries, etc. In other words, variation in barometric pressure affected the paranasal sinuses, and pain was referred to teeth with a previously produced raised irritability or decreased pain threshold. In another study, maxillary sinusitis was thought to be responsible for about 30% of barodontalgia cases (209). Mitchell (181) has reviewed many of the concepts on barodontalgia and his report should be consulted.

There is very little question that some cases of barodontalgia are associated with barosinusitis. However, there is reason to doubt that most cases of tooth pain are due to this mechanism because (1) the incidence of barotalgia in most series of experiments is greatest on ascent and barosinus pain is most frequent on descent; (2) reduced atmospheric pressure has been used with some success as a form of treatment for chronic paranasal sinusitis (45) and no cases of barodontalgia were reported but should have occurred if barosinusitis was the chief mechanism; (3) the proper filling of teeth with use of a zinc oxide–eugenol base resulted in no recurrence of pain on subsequent ascents to altitude (35, 151, 180); (4) if barosinusitis is the most important factor, one should expect a seasonal increase of barodontalgia. This has not been reported by other authors and was mentioned as not being a factor in the study by Reynolds et al. (199).

Other factors have been mentioned as a cause of barodontalgia. In areas of pathologic lesions, such as a beginning periapical abscess, there is congestion present. Even a slight gas expansion could cause pressure ischemia locally, resulting in hypoxia and pain.

It would appear that the prerequisite for barodontalgia is some type of pre-existing pathologic dental condition or at least hypersensitivity. Because tooth pain occurs at such low altitude on ascent, it would seem that local gas expansion causes pressure in the local area or produces ischemic hypoxia. It has been mentioned previously (187) that a periapical abscess can produce gas which would expand at altitude and that relief of pain could be obtained only by descent. In one case which took place in a low pressure chamber the periapical abscess ruptured and caused subsequent spreading infection which required the patient to be hospitalized. Dental extraction or dental restoration with a zinc oxide–eugenol base appears to be most effective in preventing barodontalgia. Maxillary sinusitis is probably an important cause of tooth pain at altitude and must be differentiated from true tooth pain. In should be especially suspected if the tooth pain occurs on descent.

## Time Distribution of Symptoms

Considering all the symptoms of dysbarism, it is of interest to indicate their time of occurrence in a typical exposure to high altitude. On *ascent*, the first symptoms which might appear in a *very small percentage* of individuals will be *barotalgia*, *barosinus difficulties*, or *barodontalgia*. Changes of only a few thousand feet may produce ear pain if the pharyngeal valve of the eustachian tube fails to permit equalization of pressure. Beginning at about 25,000 to 30,000 feet, a number of subjects will begin to notice the onset of such *abdominal symptoms* as bloating, eructation, and passage of gas. In the presence of gastrointestinal tract abnormalities, symptoms will occur much lower. At altitudes above 30,000 feet, abdominal distention and pain may be manifested as a frank symptom. In other words, as compared to bends, chokes, etc., abdominal symptoms occur *early* in the flight. It is very unusual for an individual to be free of abdominal symptoms on attaining the peak altitude of 38,000 feet and then develop symptoms later in the flight. However, while most cases of abdominal symptoms appear during ascent or on attaining the peak altitude, it is possible for such symptoms to become of increased severity as the flight progresses. Fortunately, the symptoms usually disappear if they are tolerated for 10 or 15 minutes at altitude.

Depending upon the amount of exercise and other factors, the highest incidence of *bends* symptoms which cause descent is manifested in the first hour at 38,000 feet (107). Swann and Rosenthal (231) found that at 38,000 feet, 28% of subjects experiencing grade 3 and 4 bends descended during the first hour and 50% more, in the second hour. If the bends were destined to become severe enough to cause descent, 50% of the individuals were forced down within 20 minutes after the first symptom and 100% within 80 minutes. The tests at 35,000 feet have shown that about 20% of all bends symptoms begin in the first 15-minute period and that about 65% are already present at the end of an hour (230). Although there are peak intervals for the appearance of bends, a very severe case of bends can develop at any time during the flight. The incidence of *chokes* at 35,000 or 38,000 feet appears to reach a peak during the second and third quarters of a 3- or

4-hour flight. Chokes can, however, develop during any period of the flight. There are obviously many factors which influence the times at which bends and chokes occur. Chokes progresses more rapidly and causes descent more frequently than bends; hence, the only general statement which may be made is that at 38,000 feet, the greatest incidence of chokes would occur in an interval of time which was somewhat later in the flight than the peak interval for bends.

Instances of *collapse at altitude* which are associated with symptoms of dysbarism, may occur at any time during a flight to 30,000 feet or above and, in a few cases, after the flight is over. Bends, chokes. or abdominal symptoms usually precede the collapse, but sometimes, the only signs and symptoms are those of pallor, faintness, or other manifestations of shock. *Central nervous system phenomena* are manifested at any time during or after flight. Paresthesia, itch, or hot and cold sensations may be noted as low as 25,000 feet, but usually do not occur until after some time at much higher altitudes (172).

On *descent*, the most common symptom is barotalgia. Barosinus difficulties also usually occur on descent. Abdominal symptoms usually completely disappear during descent. Some residual soreness may endure. Bends and chokes most often completely disappear on descent, but in a few severe cases milder manifestations have persisted for a number of hours and residual soreness has persisted for days. There have been a few instances cited previously where symptoms of bends or chokes first appeared or were exacerbated during descent. In flights at 35,000 feet, the altitude of disappearance of bends pain was related to the severity. Mild pains disappeared at about 29,000 feet, moderate pains at 26,000 feet, and severe pains at 21,000 feet (230).

## Prevention of Dysbarism

In this section we wish to consider several attempts which have been made to prevent or alleviate bends and chokes. There have been four main types of activities and a fifth which will be discussed fully in other sections: (1) denitrogenation; (2) selection

of personnel; (3) use of drugs; (4) use of an altitude pressure bag; and (5) development of pressure cabin aircraft which was designed to prevent hypoxia but also aided in resolving the problem of dysbarism.

**Denitrogenation.** Gray (103) has discussed denitrogenation and its effects on altitude dysbarism. Many other references to the subject are contained in several publications (16, 34, 82, 129, 133, 134).

If bends and chokes are caused by the formation of nitrogen bubbles, then the elimination of nitrogen from the body prior to exposure and before it can form bubbles should prevent the symptoms. To effect a reduction of nitrogen in the body, decompression may be performed very slowly so as to allow time for the excess body nitrogen to escape, or high concentrations of oxygen can be inspired for varying intervals of time.

Slow decompression to effect denitrogenation has been used by sea divers for about 100 years. Rather than slow, continuous decompression, Haldane in 1908 introduced a most important concept, that of decompression in stages. He demonstrated that decompression in stages produced a larger gradient between the pressures of nitrogen inside and outside the body and, thereby, increased the elimination rate of nitrogen. This prevents tissue supersaturation with nitrogen and, thus, the tendency of the gas to produce bubbles.

If 100% oxygen is inspired at ambient pressure, then the intake of nitrogen is zero, but the expired air contains nitrogen derived from the body fluids and tissues. In time, the body nitrogen is depleted. The total process is properly emphasized by the term "denitrogenation" rather than "preoxygenation." It is the elimination of nitrogen which is important, and not a special benefit of oxygen per se, except in the sense that during denitrogenation one is substituting a metabolizable gas for nitrogen.

The use of 100% oxygen to effect denitrogenation of the body is far more applicable to the prevention of altitude symptoms than

in the case of caisson workers or divers. This is due to the toxicity of oxygen at high pressures in the latter case, whereas 100% oxygen at high altitude can be breathed safely for relatively long intervals.

The rate at which nitrogen is eliminated from the body has been studied by a number of investigators whose results have been reviewed by Catchpole and Gersh (51). About one-half of the body nitrogen is contained in the fatty tissues of an individual whose fat content is 15 to 20% of his body weight (22, 28, 47). During decompressions of short duration, the body fat may act as a reservoir to protect the body against the sudden release of nitrogen and bubble formation (22). Typical nitrogen desaturation curves obtained by Behnke et al. (28) reveal a number of important facts: (1) the weight of nitrogen dissolved in the body varies directly with the $P_{N_2}$ in the inspired air. This would be expected on the basis of Henry's law, since nitrogen is an inert gas in the body and does not combine with such agents as hemoglobin, as does oxygen; (2) the time required for denitrogenation is equal to the time required for renitrogenation; (3) the rate of nitrogen elimination in terms of volume per unit time is a direct function of the gradient of nitrogen tension between the inside and the outside of the body. This means that if the nitrogen tension of the inspired air were reduced to zero, the rate of its elimination would be twice as fast as it would be if its tension were only reduced 50%.

There are other features of the denitrogenation curves which are of interest. The measurements which have been made show that denitrogenation is most rapid (in terms of cubic centimeters eliminated per minute) at the beginning and then reaches a zero rate after about 6 to 8 hours; 50% denitrogenation is accomplished in about 30 minutes.

Different parts of the body denitrogenate at different rates. Ferris et al. (73) found that the arterial blood denitrogenates rapidly, requiring less than 5 minutes to lose 90% of its nitrogen. It would also require about 5 minutes to regain its nitrogen if the person was returned to breathing air. Venous blood also denitrogenates rapidly, but slower than arterial blood. Cerebrospinal

fluid, synovial fluid, etc., denitrogenate more slowly. The barrier to nitrogen elimination from the body is not in the lungs but is between the tissues and the venous blood. While nitrogen is more soluble in fat, the probable reason why fat serves as a reservoir for nitrogen much better than it ordinarily should is because the capillary circulation through fat is relatively inadequate (89). Because of circulatory factors, small animals are in general much more resistant to dysbarism than are large animals. It is of interest that the rate of nitrogen elimination differs significantly between individuals and in the same individual from day to day, and that the subjects with a high rate of nitrogen elimination are generally more resistant to bends, chokes, etc., than are other subjects (223, 224).

A large number of interrelated physiologic mechanisms determine susceptibility to bends and chokes. There are so-called "normal" ranges of capillary surface in tissues, blood flow, fat deposition in organs, rates of gas exchanges, etc. In explaining the differences between individual susceptibilities to bends and chokes, the concept of variations in gas exchange and other of these factors may be important. For example, if nitrogen gas is important in bubble formation, then the rate at which a "normal" person denitrogenates various tissues when breathing oxygen may be the difference between no bends at altitude, and mild, moderate, or severe bends. In essence, this may mean that gas exchange across the gas-blood barrier in the lungs and the blood-tissue fluid barriers in the metabolizing tissues is such in different individuals, or in the same individual during various times and stresses, that they are more or less rendered susceptible to bends. In the exchange of gases across the lungs of normal young subjects, it was concluded that the gas-blood barrier exchange of inert gases was not nearly as important as was the renewal of gases by pulmonary ventilation, the gas solubility, and the *effective blood flow* through the lungs (148). In the tissues, it was also the blood-tissue perfusion factor rather than a difference in diffusion of gas which was important. Different types of tissue have different rates of blood flow per unit of tissue. The capillary surface of fatty tissue is relatively inadequate as compared to muscle or other tissues (89). In effect, this means that it is possible that the additional amount

of nitrogen dissolved in fatty tissue is not as important to bubble formation under some conditions as is the decreased amount of capillary surface area available for blood-tissue perfusion.

Denitrogenation of humans by breathing increased percentages of oxygen has proved to be markedly effective in the prevention of altitude dysbarism. The chief disadvantages are the expense involved and the periods of time in which the individuals must denitrogenate to obtain significant protection. Ferris et al. (76) found that approximately 4 hours of inhalation of 100% oxygen were necessary to completely protect the more susceptible individuals who were expected to exercise at 35,000 feet. One or 2 hours of oxygen inhalation offered more complete protection from bends than from chokes. Prophylactic treatment of subjects exposed to 35,000 feet by inhalation of oxygen for 9 hours protected 71% completely, even though there was an air-breathing interval as long as 5 hours between the inhalation and the ascent (19, 239). For very susceptible individuals, it was advised that the period of re-exposure to air should be shortened. This finding emphasized that the period of renitrogenation was about as long as the period of denitrogenation. There was also good correlation with Behnke's observations that the individuals who desaturated slowly also resaturated slowly.

It was theorized that exercise performed along with preflight denitrogenation should give added protection since exercise, by increasing peripheral blood flow and cardiac output, would accelerate the elimination of nitrogen (253). In the cited study, strenuous exercise combined with preflight oxygen administration gave added protection against dysbarism. Other investigations have not supported this contention, and Gray (103) has summarized School of Aviation Medicine data to show that the inclusion of exercise did not contribute to the prevention of symptoms, and any possible benefits therefrom were overshadowed by the disadvantage of the resulting fatigue as well as the possible loss of thermal insulation of flying clothing due to sweating. His data show that the incidence of bends and chokes in 76 control subjects exposed to 38,000 feet for 2 hours was 25%. In 87 subjects who

denitrogenated for 45 minutes before ascent there was an incidence of 2.3%, whereas in 88 subjects who denitrogenated for 45 minutes while exercising, the incidence was 4.6%.

In an attempt to make denitrogenation procedures as practical as possible, it was desirable to determine the shortest denitrogenation procedures which would be effective and, also, whether denitrogenation was effective when performed at altitude (tables XXXI, XXXII). The data taken from studies by Gray (98, 101) confirm the views of Behnke (24) that denitrogenation at altitude is effective.

In the experiments to determine the effectiveness of denitrogenation while at altitude, aviation cadets were given a 2-hour flight at 38,000 feet preceded by a 15-minute period of leveling off at

## TABLE XXXI

*Increasing the duration of denitrogenation*

| Denitrogenation period (min.) | Man-flights | Percent descents due to bends and chokes | Percent protection |
|---|---|---|---|
| 0 | 223 | 25.2 | 0 |
| 15 | 204 | 11.8 | 53 |
| 30 | 145 | 6.2 | 75 |
| 45 | 180 | 3.4 | 87 |

## TABLE XXXII

*Denitrogenation at various altitudes*

| Altitude of denitrogenation | Man-flights | Percent descents due to bends and chokes | Percent protection |
|---|---|---|---|
| Controls | 950 | 24.4 | 0 |
| Ground level | 204 | 11.8 | 52 |
| 15,000 ft. | 181 | 10.0 | 59 |
| 20,000 ft. | 205 | 10.8 | 56 |
| 25,000 ft. | 290 | 15.2 | 38 |
| 30,000 ft. | 224 | 16.1 | 34 |
| 38,000 ft. | 727 | 25.2 | -3 |

various altitudes. During this time, the subjects breathed 100% oxygen at the ambient pressure of the particular altitude.

These results revealed that breathing 100% oxygen up to about 20,000 feet was about as effective in giving protection against bends and chokes as denitrogenation at ground level. This is a most practical finding, since the interference of denitrogenation procedures with takeoff preparations can be avoided; that is, if sufficient oxygen can be carried, the crew can be denitrogenated by a planned pattern of ascent to altitude.

The use of pressure breathing at altitude was primarily introduced to attain higher altitudes by combating hypoxia more effectively. In several series of tests (139, 142, 143), the data on individuals (rather than on the group as a whole) suggest that pressure breathing exerts a protective effect against bends. Some tests may be so severe that any beneficial effect is masked. In the experience of the Ivy group (143), at least one very susceptible individual was able to stay at 38,000 feet for 2 hours with exercise on 2 occasions while pressure breathing, whereas he was 100% susceptible on more than 60 other exposures using constant flow or demand oxygen equipment. The impression of several of the investigators with much experience in the low pressure chamber was that pressure breathing increased their own tolerance to bends at altitudes above 40,000 feet. The introduction of exercise at altitude may constitute the difference since the incidence of bends was somewhat less in subjects seated at 47,500 feet for 1 hour using intermittent pressure breathing than in subjects seated at 38,000 feet for 2 hours or 40,000 feet for 1 hour using continuous flow or demand oxygen equipment. Hyman and North (139) also found that some individuals showed a gain in tolerance. The conservative conclusion in both series of tests was that pressure breathing did not offer clear-cut protection of all individuals. Gray's data (100) showed that trained subjects did slightly better than untrained subjects when they used pressure breathing, but the differences were not considered significant.

If we can assume that some individuals obtain a beneficial effect, then the explanation may be that pressure breathing hyperventilated the subjects and in reducing their $P_{CO_2}$ possibly retarded

bubble growth or altered the circulation in tissues. It may also be true that pressure breathing promotes denitrogenation through hyperventilation. These are possible explanations for one study at 40,000 feet (44) where deliberate hyperventilation reduced the incidence of intolerable bends from 20 to 8%.

The procedure of denitrogenation is effective in the prevention of altitude dysbarism. However, the factors which influence the incidence of bends and chokes still apply. The older the individual, the longer he would need to be denitrogenated in order to obtain the same degree of protection as a younger man. The higher the altitude and the more strenuous the exercise at altitude, the longer the time of denitrogenation necessary for protection. As a general rule, the more susceptible the individual, the longer will be the necessary period of denitrogenation.

In passing, it is obvious that the effectiveness of denitrogenation in preventing bends and chokes is the strongest single evidence in support of the bubble theory or etiology. Other evidence, however, does support the conclusion that the circulation is a contributing factor.

**Selection of immune personnel.** The low pressure chamber was initially conceived as being useful for (1) training flying personnel in the effects of altitude and the use of oxygen equipment, and (2) classifying personnel with regard to their susceptibility to dysbarism and hypoxia.

At the present time, the low pressure chamber is used chiefly for indoctrination and training research and, occasionally, to determine unusually low thresholds of tolerance for hypoxia. After a considerable amount of experimentation, it was advised that the goal of classifying flying personnel as to their susceptibility to dysbarism, except in special instances, should be abandoned (63). The testing of individuals was expensive and, except for special circumstances, unnecessary. Altitude dysbarism was very uncommon in the field since very little flying was being performed at altitudes where the highest incidence of dysbarism occurred (18, 55). A second reason was that the usual flight patterns included a prolonged period of ascent so that the resulting denitrogenation afforded adequate protection against bends and chokes (103).

It is instructive, however, to note several aspects of the problem as it presented itself in March 1942. First of all, it soon became obvious that any classification scheme would require more than one test at altitude. In fact, even 5 consecutive flights taken by 43 aviation cadets revealed a striking inconsistency of performance (106); 44% of the subjects completed all 5 flights and 2% consistently failed all 5 flights. The remaining 54% were erratic in their performance. This picture was further complicated by several facts. If enough flights are made, probably no individual is 100% resistant or susceptible. While symptoms of bends and chokes tended to recur, there were other symptoms such as abdominal pain, barotalgia, barodontalgia, etc., which showed comparatively little tendency to recur. Occasionally, an individual would be found who was forced to descend repeatedly because of abdominal symptoms. One case was later diagnosed as cardiospasm.

In other words, it would have been necessary to perform a large number of tests to classify individuals and, for most individuals, the testing procedures were unreliable. The best that could have been accomplished was to weed out a small number of highly susceptible individuals.

At various intervals, the classification procedures have been revised by increasing the altitude, reducing the duration of time at altitude, introducing a standard exercise or increasing the number of ascents (97, 105, 106, 126, 202, 211, 258).

It is certain that increasing the number of flights makes the data more reliable, if the individual is not penalized for being forced to descend because of gas pains, toothache, or other deficiencies which are remedial. It was found that selection of individuals as being resistant by using either height or weight was as efficient as selection by 1, but not 2, low pressure chamber tests (163).

Of interest in regard to increasing the validity of results by multiple exposure, are the data obtained on 7 subjects who were exposed to 38,000 feet from 47 to 69 times (42). All tests were

begun after 6 p.m. and there were 3 exposures to altitude each week. These subjects were variably susceptible to bends ranging from 33 to 94% with an average of 67%. The important fact is that when the data were tabulated in groups of 10 successive tests, then the average susceptibility varied from 45 to 80%. These experiments indicate the difficulties in determining the effect of single factors on an individual's susceptibility to bends, and again raises the question of validity in classifying most flying personnel on the basis of their tolerance to bends.

The introduction of pressure cabin aircraft has reduced the necessity for classifying all individuals as to their tolerance of dysbarism. In the event of a sudden loss of pressurization, the rapid onset of bends, chokes, and abdominal symptoms will be secondary problems to that of hypoxia. It should be recognized, however, that in special cases the circumstances may be such that an individual who is abnormally susceptible to symptoms of dysbarism at 25,000 or 30,000 feet could endanger a mission. A beforehand knowledge of relative individual susceptibility in these cases may be advisable, and it should be of obvious value to determine the susceptibility of key personnel after they had been denitrogenated for a practical period of time.

**Use of drugs.** A number of drugs have been administered to subjects preflight or during flight in low pressure chambers to determine their effects on the prevention and tolerance of bends symptoms.

Aminophylline has been used in an attempt to alter circulation and alleviate bends at altitude. Some success with this method was reported (160, 161). Morphine has been investigated as an analgesic for bends in case descent could not be effected (57, 221, 222). It was not effective. The administration of 10 mg. of dextroamphetamine to 50 subjects 1.5 to 2 hours prior to ascent to 40,000 feet for 1 hour with no exercise at altitude decreased the incidence of incapacitating bends and chokes from 32.4 to 14%. The total incidence of bends and chokes was not significantly reduced (141). It was thought that the dextroamphetamine may have increased the general circulation, but acted chiefly by im-

proving the feeling of well-being, decreasing apprehension, and exaggerating the "willingness to endure" symptoms. In the same report it was shown that dextroamphetamine, plus a 30- to 45-minute period of denitrogenation, reduced the incidence of incapacitating bends and chokes from 32.4 to 0%, and reduced the incidence of all cases of bends from 54.3 to 24%. Contrary to the above findings, Ryder et al. (207) were unable to confirm the favorable effect of dextroamphetamine on the incidence of bends. A number of other drugs and drug combinations were tested by the Ivy group for their effect on bends. These included thyroid extract, aspirin, aspirin-phenacetin-caffeine, and several others (42). Canadian investigators (240) reported that the administration of adrenalin, aspirin, and papaverine produced no significant changes in the incidence of dysbarism, but it is noteworthy that there was a slightly higher incidence of symptoms on the day following a heavy intake of alcohol.

In summary, the use of drugs practically in the prevention of bends has led to disappointing results. However, studies conducted with some of the newer compounds may still be worthwhile, and such experiments could aid in further elucidation of the mechanism of bends.

**Pressure bag.** One procedure to treat bends and chokes in single crew members should be mentioned. In combat, it was conceivable that a crew member might develop severe symptoms, but the conditions could be such that descent of the aircraft to lower altitudes would be dangerous. An altitude pressure bag was designed to afford relief of bends in an aircraft (84). The affected individual was placed in the pressure bag which was then inflated by an air compressor. At an altitude of 30,000 feet the bag could be kept at an effective altitude of about 15,000 feet. In addition, the bag was equipped with an oxygen regulator, headset, and electrically heated suit circuit. On tests up to 40,000 feet the relief of bends was found to be immediate upon application of pressure to the bag. When pressure was released, the bends returned, if the subject was still at high altitude.

**Pressure cabin aircraft.** The maintenance of a low cabin pressure altitude while the aircraft attains a much higher pressure altitude has been effective in preventing hypoxia as well as symptoms of altitude dysbarism.

## REFERENCES


1. Adler, H. F., A. J. Atkinson, and A. C. Ivy. Effect of morphine and Dilaudid on the ileum and of morphine, Dilaudid and atropine on the colon of man. Arch. Intern. Med. 69:974 (1942).

2. Adler, H. F., A. J. Atkinson, and A. C. Ivy. A study of motility of the human colon: An explanation of "dysynergia" of the colon or of the unstable colon. Amer. J. Dig. Dis. 8:197 (1941).

3. Adler, H. F., A. J. Atkinson, and A. C. Ivy. Supplementary and synergistic action of stimulating drugs on the colon motility. Surg. Gynec. Obstet. 74:809 (1942).

4. Adler, H. F., J. M. Beazell, A. J. Atkinson, and A. C. Ivy. The motor response of the colon to alcohol. Quart. J. Stud. Alcohol 1:638 (1941).

5. Adler, H. F., and F. S. Grodins. Abdominal symptoms at altitude. AAF School of Aviation Medicine Report 493-1, June 1947.

6. Allan, J. H. Traumatic calcifications: A precipitating factor in "bends" pain. J. Aviation Med. 16:235 (1945).

7. Alvarez, W. C. An introduction to gastroenterology, 3d ed., p. 577. New York: Paul B. Hoeber, 1941.

8. Alvarez, W. C. What causes flatulence? J. A. M. A. 120:21 (1942).

9. Anderson, K., and A. Ringsted. Clinical and experimental investigations on ileus with particular reference to genesis of intestinal gas. Acta Chir. Scand. 88:475 (1943).

10. Anthony, R. A., R. W. Clarke, A. Liberman, L. F. Nims, J. Tepperman, and S. M. Wesley. Effects of local compression, impairment of venous return and arterial tourniquet upon the intensity of established "bends" pain. CAM Report No. 143, 16 June 1943.

11. Anthony, R. A., R. W. Clarke, A. Liberman, L. F. Nims, J. Tepperman, and S. M. Wesley. Temperature and decompression sickness. CAM Report No. 136, 26 May 1943.

12. Armstrong, H. G. Analysis of gas emboli. Eng. Sec. Mem. Rep., EXP-M-54-653-3, Wright Field, 20 Dec. 1939.

13. Armstrong, H. G. The development of caisson disease at high altitude. Eng. Sect. Mem. Rep., Q-54-59, Wright Field, 24 Feb. 1938.

14. Armstrong, H. G. The effects of decreased barometric pressures on the living organism. Eng. Sect. Mem. Rep., Q-54-62, Wright Field, 25 Mar. 1938.

15. Armstrong, H. G. Our present physical standard for flying. J. Aviation Med. 5:107 (1934).

16. Armstrong, H. G. Principles and practice of aviation medicine. Baltimore: Williams and Wilkins, 1939.

17. Armstrong, H. G., and J. W. Heim. The effect of flight on the middle ear. J. A. M. A. 109:417 (1937).

18. Bachrach, W. H. Information obtained from high altitude combat veterans. Av. Phy. Bull. No. 7, Sept. 1944.

19. Bazett, H. C., J. W. Thompson, and J. B. Bateman. The prevention of decompression sickness in susceptible individuals. Proc. of Meeting on Aviation Medical Research, NRC, June 1942.

20. Beazell, J. M., and A. C. Ivy. The quantity of colonic flatus excreted by the "normal" individual. Amer. J. Dig. Dis. 8:128 (1941).

21. Behnke, A. R. The absorption and elimination of gases of the body in relation to its fat and water content. Medicine 24:359 (1945).

22. Behnke, A. R. The application of measurements of nitrogen elimination to the problem of decompressing divers. U.S. Nav. Med. Bull. 35:219 (1937).

23. Behnke, A. R. High atmospheric pressures; physiological effects of increased and decreased pressure; application of these findings to clinical medicine. Ann. Intern. Med. 13:2217 (1940).

24. Behnke, A. R. Investigations concerned with problems of high altitude flying and deep diving. Milit. Surg. 90:9 (1942).

25. Behnke, A. R. Physiologic studies pertaining to deep sea diving and aviation, especially in relation to the fat content and composition of the body. Harvey Lect. 37:198 (1942).

26. Behnke, A. R. A review of physiologic and clinical data pertaining to decompression sickness. U.S. Nav. Med. Res. Inst. Res. Rep. No. 4, Project X-443, 13 May 1947.

27. Behnke, A. R., B. G. Feen, and W. C. Welham. The specific gravity of healthy men. J. A. M. A. 118:495 (1942).

28. Behnke, A. R., R. M. Thomson, and L. A. Shaw. The rate of elimination of dissolved nitrogen in man in relation to the fat and water content of the body. Amer. J. Physiol. 114:137 (1935).

29. Behnke, A. R., W. Welham, and O. D. Yarbrough. The value of preliminary oxygen inhalation for the prevention of decompression sickness during high altitude flight. CAM Report No. 114, 15 Dec. 1942.

30. Behnke, A. R., and T. L. Willmon. Physiological effects of high altitude. U.S. Nav. Med. Bull. 39:163 (1941).

31. Bierman, H. R., H. A. Smedal, and C. L. Gemmill. The after-effects of exposure to lowered barometric pressure. CAM Report No. 78, 17 Aug. 1942.

32. Bierman, H. R., H. A. Smedal, and C. L. Gemmill. The incidence of decompression illness in the classification of aviation personnel. CAM Report No. 65, 18 Aug. 1942, and CAM Report No. 88, 23 Sept. 1942.

33. Blair, H. A., R. J. Dern, and W. O. Fenn. Abdominal gas. CAM Report No. 193, 7 Oct. 1943.

34. Boycott, A. E., G. C. C. Damant, and J. S. Haldane. The prevention of compressed air illness. J. Hyg. (London) 8:342 (1908).

35. Brickman, I. W. Toothache in the low pressure chamber. U.S. Nav. Med. Bull. 43:292 (1944).

36. Bridge, E. V., F. M. Henry, S. F. Cook, O. L. Williams, W. R. Lyons, and J. H. Lawrence. Decompression sickness. J. Aviation Med. 15:316 (1944).

37. Bridge, E. V., F. M. Henry, O. L. Williams, and J. H. Lawrence. "Chokes": A respiratory manifestation of aero-embolism in high altitude flying. Ann. Intern. Med. 22:398 (1945).

38. Brown, B. R. The incidence and relation of syncope to decompression sickness. J. Aviation Med. 17:257 (1946).

39. Brown, G. A., C. H. Cronick, H. L. Motley, E. J. Kocour, and W. O. Klingman. Nervous system dysfunction in adaptation to high altitude and post flight reactions. War Med. 7:157 (1945).

40. BuMed News Letter, Div. of Aviation Medicine, Navy Department Aviation Supplement, vol. 9, No. 2, 1948.

41. Burkhart, T. M. Decreased tolerance to bends. Hospital Corps Quarterly, U.S. Navy, 18:38, May 1945.

42. Burkhardt, W. L., H. F. Adler, A. F. Thometz, A. J. Atkinson, and A. C. Ivy. Decompression sickness. J. A. M. A. 133:373 (1947).

43. Burkhardt, W. L., H. F. Adler, A. F. Thometz, A. J. Atkinson, and A. C. Ivy. A Roentgenographic study of "bends" and "chokes" at altitude. J. Aviation Med. 17:462 (1946).

44. Burkhardt, W. L., A. F. Thometz, and A. C. Ivy. The effect of deliberate hyperventilation on the incidence of "intolerable" cases of bends and chokes. CAM Report No. 438, June 1945.

45. Butler, D. B., G. J. Greenwood, and A. C. Ivy. Reduced atmospheric pressure as a form of treatment for paranasal sinusitis. Arch. Otolaryng. (Chicago) 40:266 (1944).

46. Campbell, J. A. The carbon dioxide partial pressure in body cavities and tissue spaces under various conditions. J. Physiol. (London) 57:273 (1923).

47. Campbell, J. A., and L. Hill. Concerning the amount of nitrogen gas in the tissues and its removal by breathing almost pure oxygen. J. Physiol. (London) 71:309 (1931).

48. Cannon, W. B. The nature of gastric peristalsis. Amer. J. Physiol. 29:250 (1911).

49. Catchpole, H. R., and I. Gersh. Bubble formation in rabbits decompressed to altitude: Effect of preoxygenation, electrical stimulation, and some pharmacological factors. J. Cell. Comp. Physiol. 27:27 (1946).

50. Catchpole, H. R., and I. Gersh. Pathogenetic factors and pathological consequences of decompression sickness. Physiol. Rev. 27:360 (1947).

51. Catchpole, H. R., and I. Gersh. Physical factors in the pathogenesis of aero-embolism: A review. Naval Med. Research Inst. Project X-284, 26 Apr. 1946.

52. Catchpole, H. R., and I. Gersh. Physiological factors affecting the production of gas bubbles in rabbits decompressed to altitude. J. Cell. Comp. Physiol. 27:15 (1946).

53. Chapman, W. P., and C. M. Jones. Variations in cutaneous and visceral pain sensitivity in normal subjects. J. Clin. Invest. 23:81 (1944).

54. Coley, B. L., and M. Moore. Caisson disease with special reference to bone and joints: Report of two cases. Ann. Surg. 111:1065 (1940).

55. Collias, N. E., and W. H. Bachrach. Decompression sickness in combat. Aeromedical Laboratory TSEAL 3-697-24, 29 May 1945.

56. Collins, L. H., Jr. Excessive abdominal distention at high altitudes in case of congenital megacolon (Hirschsprungs Disease). J. A. M. A. 117:1012 (1941).

57. Comroe, J. H. The use of morphine and Demerol for the relief of pain of bends. CAM Report No. 198, Sept. 1943.

58. Cook, S. F., O. L. Williams, W. R. Lyons, and J. H. Lawrence. A comparison of altitude and exercise with respect to decompression sickness. War Med. 6:182 (1944).

59. Cullen, G. E., and I. Earle. Studies of acid-base equilibrium of blood: Physiological changes in acid-base condition throughout the day. J. Biol. Chem. 83:545 (1929).

60. DeVoe, K., and H. L. Motley. Aerodontalgia. Dent. Dig. 51:1[illegible] (1945).

61. Dill, D. B. Fatigue induced by repeated exposures to low pressures. EXP-M-54-653-61, 3 Oct. 1941.

62. Dill, D. B. Observations on acid-base balance and fatigue in high altitudes. CAM Report No. 80, 10 June 1941.

63. Dill, D. B. Resistance to aero-embolism. Aero-Medical Laboratory Project ENG-M-49-696-1D, 29 Mar. 1943.

64. Drefus, H. Les dents des aviateurs. L'Odontologie 75:612 (1937).

65. Edelmann, A., W. V. Whitehorn, and F. A. Hitchcock. The effects of explosive decompression on human subjects. Fed. Proc. 5:24 (1946).

66. End, E. The physiologic effects of increased pressure. Proc. Sixth Pacific Science Congress, 6:91 (1939).

67. Engel, G. L., J. Romano, J. P. Webb, E. B. Ferris, M. A. Blankenhorn, and H. W. Ryder. Scotoma, blurring of vision, and headache as complications of decompression sickness. CAM Report No. 127, 5 Apr. 1943.

68. Erdman, S. The acute effects of caisson disease on aeropathy. Amer. J. Med. Sci. 145:520 (1913).

69. Evelyn, K. A. Effects of low barometric pressure on the health of the adult male in the age group 19-32. CAM Report No. 19, 3 July 1941.

70. Evelyn, K. A. The effect of simulated high altitudes on human subjects. Report No. 1, London Association for War Research, University of Western Ontario. Report to NRC, Apr. 1941.

71. Evelyn, K. A. The effect of simulated high altitudes on human subjects. Report No. 2, London Association for War Research, University of Western Ontario. Report to NRC, July 1941.

72. Evelyn, K. A. The effect of simulated high altitudes on human subjects. Report No. 3, London Association for War Research, University of Western Ontario, Proceedings of Associate Committee on Aviation Medical Research, NRC, Sept. 1941.

73. Ferris, E. B., W. E. Molle, and H. W. Ryder. Nitrogen exchange in tissue components of man. CAM Report No. 60, 15 July 1942.

74. Ferris, E. B., J. P. Webb, G. Engel, and E. V. Brown. A comparative study of decompression sickness under varied conditions of exercise, altitude and denitrogenation. CAM Report No. 363, 18 July 1944.

75. Ferris, E. B., J. P. Webb, H. W. Ryder, G. L. Engel, J. Romano, and M. A. Blankenhorn. The importance of straining movements in electing the site of bends. CAM Report No. 121, 16 Feb. 1943.

76. Ferris, E. B., J. P. Webb, H. W. Ryder, G. L. Engel, J. Romano, and M. A. Blankenhorn. The protective value of preflight oxygen inhalation at rest against decompression sickness. CAM Report No. 132, 1 Apr. 1943.

77. Fine, J., J. B. Sears, and B. M. Banks. The effect of oxygen inhalation on gaseous distention of the stomach and the small intestine. Amer. J. Dig. Dis. 2:361 (1935).

78. Fraser, A. M. The effect of rate of decompression on the incidence of decompression sickness at low temperature. Number 1 Clinical Investigation Unit, RCAF, Toronto. Proceedings of the Associate Committee on Aviation Medicine Research, NRC, Apr. 1942.

79. Fraser, A. M., C. B. Stewart, and G. W. Manning. Review of Canadian investigations on decompression sickness. Number 2 Clinical Investigation Unit, RCAF, Regina. Also Flying Personnel Medical Section. Number One "Y" Depot, RCAF, Halifax. Report to NRC, June 1943.

80. Fraser, A. M., and E. T. Waters. The effect of hydrostatic pressure on the amelioration of symptoms of decompression sickness. Number 1 Clinical Investigation Unit, RCAF, Toronto. Proceedings of Associate Committee on Aviation Medical Research, NRC, 10 July 1942.

81. Fries, J. A. Intestinal gases of man. Amer. J. Physiol. 16:468 (1906).

82. Fulton, J. F. Aviation medicine in its preventive aspects. London: Oxford University Press, 1948.

83. Fulton, G. P., and S. Phillips. Analysis of symptoms causing forced descents in the altitude chambers at the San Antonio Aviation Cadet Center. J. Aviation Med. 17:244 (1946).

84. Gagge, A. P. Altitude pressure bag. CAM Report No. 186, 27 July 1943.

85. Gersh, I. Correlation of x-ray and gross observations on gas bubbles in guinea pigs decompressed from high pressure atmospheres. J. Gen. Physiol. 28:271 (1946).

86. Gersh, I. Gas bubbles in bone and associated structures, lung and spleen of guinea pigs decompressed rapidly from high pressure atmospheres. J. Cell. Comp. Physiol. 26:101 (1945).

87. Gersh, I., and H. R. Catchpole. Appearance and distribution of gas bubbles in rabbits decompressed to altitude. J. Cell. Comp. Physiol. 28:253 (1946).

88. Gersh, I., G. E. Hawkinson, and E. H. Jenney. Comparison of vascular and extravascular bubbles following decompression from high pressure atmospheres of oxygen, helium-oxygen, argon-oxygen and air. J. Cell. Comp. Physiol. 26:63 (1945).

89. Gersh, I., and M. A. Still. Blood vessels in fat tissue: Relation to problems of gas exchange. J. Exp. Med. 81:219 (1945).

90. Gersh, I., and M. A. Still. Relations of capillaries to fat cells. Naval Med. Research Inst. Project X-284, Rep. No. 3, 12 Sept. 1944.

91. Gesell, R. On the chemical regulation of respiration. Amer. J. Physiol. 66:5 (1923).

92. Goldhush, A. A. A dental survey of fighter pilots. Air Surg. Bull. 2:436 (1945).

93. Goldhush, A. A. Oral aspects of aviation medicine. *In* Burket, L. W. Oral medicine. Philadelphia: J. B. Lippincott, 1946.

94. Gordon, J. O., and C. H. Heacock. Roentgenologic demonstration of localized gas in caisson disease. J. A. M. A. 114:570 (1940).

95. Gouze, F. J. Air embolism in a diver. U.S. Nav. Med. Bull. 43:538 (1944).

96. Gray, J. S. Aero-embolism induced by exercise in cadets at 23,000 feet. AAF School of Aviation Medicine Report 227-1, Jan. 1944.

97. Gray, J. S. Certain advantages of a simulated flight at 38,000 feet for high altitude classification. AAF School of Aviation Medicine Report 14-1, Sept. 1942.

98. Gray, J. S. Effect of denitrogenation at various altitudes on aero-embolism in cadets. AAF School of Aviation Medicine Report 216-1, Jan. 1944.

99. Gray, J. S. The effect of exercise at altitude on aero-embolism in cadets. AAF School of Aviation Medicine Report 156-1, June 1943.

100. Gray, J. S. The effects of pressure breathing on decompression sickness and circulatory reactions in cadets. CAM Report No. 287, 15 Mar. 1944.

101. Gray, J. S. The effect of varying periods of denitrogenation on aero-embolism in cadets. AAF School of Aviation Medicine Report 164-1, June 1943.

102. Gray, J. S. The location, severity, and altitude of disappearance of the bends. AAF School of Aviation Medicine Report 117-1, Feb. 1943.

103. Gray, J. S. Present status of the problem of decompression sickness. AAF School of Aviation Medicine Report 458-1, Jan. 1946.

104. Gray, J. S. The prevention of aero-embolism by denitrogenation procedures. AAF School of Aviation Medicine Report 101-1, Dec. 1942.

105. Gray, J. S. The reliability of procedures for high altitude classification. AAF School of Aviation Medicine Report 70-1, Nov. 1942.

106. Gray, J. S. Symptoms experienced during repeated low pressure chamber flights and their significance for high altitude classification. AAF School of Aviation Medicine Report 57-1, July 1942.

107. Gray, J. S. The time-distribution of symptoms at 35,000 and 38,000 feet in the low pressure chamber. AAF School of Aviation Medicine Report 71-1, Sept. 1942.

108. Gray, J. S., and S. C. F. Mahady. The prevention of aero-embolism in cadets at 45,000 feet by denitrogenation. CAM Report No. 315, 29 Mar. 1944.

109. Gray, J. S., S. C. F. Mahady, R. L. Masland, and H. S. Wigodsky. Studies on altitude decompression sickness: I. Symptomatology. J. Aviation. Med. 17:333 (1946).

110. Gray, J. S., R. L. Masland, and S. C. F. Mahady. The effect of breathing carbon dioxide in oxygen on altitude decompression sickness. AAF School of Aviation Medicine Report 409-1, July 1945.

111. Griffin, D. R., S. Robinson, H. S. Belding, R. C. Darling, and E. S. Turrell. The effects of cold and rate of ascent on aero-embolism. J. Aviation Med. 17:56 (1946).

112. Griffin, D. R., S. Robinson, H. S. Belding, R. C. Darling, E. Turrell, and F. Consolagio. The effects of cold and rate of ascent on aero-embolism. CAM Report No. 174, 22 June 1943.

113. Grodins, F. S., A. C. Ivy, and H. F. Adler. Intravenous administration of oxygen. J. Lab. Clin. Med. 28:1009 (1943).

114. Guest, M. M. The incidence of bends during different periods of the day. Air Surg. Bull. 1:5 (June 1944).

115. Harris, M., W. E. Berg, D. M. Whitaker, and V. C. Twitty. The relation of exercise to bubble formation in animals decompressed to sea level from high barometric pressures. J. Gen. Physiol. 28:241 (1945).

116. Harris, M., W. E. Berg, D. M. Whitaker, V. C. Twitty, and L. R. Blinks. Carbon dioxide as a facilitating agent in the initiation and growth of bubbles in animals decompressed to simulated altitudes. J. Gen. Physiol. 28:225 (1945).

117. Harvey, E. N. Bubble formation in animals. CAM Report No. 469, Oct. 1945.

118. Harvey, E. N. Decompression sickness and bubble formation in blood and tissues. Bull. N.Y. Acad. Med. (New Series) 21:505 (1945).

119. Harvey, E. N., D. K. Barnes, W. D. McElroy, A. H. Whiteley, D. C. Pease, and K. W. Cooper. Bubble formation in animals: I. Physical factors. J. Cell. Comp. Physiol. 24:1 (1944).

120. Harvey, E. N., W. D. McElroy, D. C. Pease, A. H. Whiteley, G. Warren, D. K. Barnes, and W. Kleinberg. The mechanism of bubble formation in the blood of mammals in relation to decompression sickness. CAM Report No. 229, 25 Oct. 1943.

121. Harvey E. N., W. D. McElroy, A. H. Whiteley, G. H. Warren, and D. C. Pease. Bubble formation in animals: III. An analysis of gas tension and hydrostatic pressure in cats. J. Cell. Comp. Physiol. 24:117 (1944).

122. Harvey, E. N., A. H. Whiteley, W. D. McElroy, D. C. Pease, and D. K. Barnes. Bubble formation in animals: II. Gas nuclei and their distribution in blood and tissues. J. Cell. Comp. Physiol. 24:23 (1944).

123. Heath, E. M. Altitude chamber as a diagnostic aid. Air Surg. Bull. 1:1 (1944).

124. Henry, F. M. Altitude pain. J. Aviation Med. 17:[illegible] (1946).

125. Henry, F. M., S. F. Cook, E. Strajman, and D. W. Lund. Effectiveness of pre-flight oxygen breathing in preventing decompression sickness. CAM Report No. 384, Oct. 1944.

126. Henry F. M., H. B. Jones, J. B. Mohney, and C. A. Tobias. The reliability of decompression chamber classification using step-up exercise and the reliability of inert gas exchange and other factors of bends resistance. CAM Report No. 264, 2 Sept. 1943.

127. Henry, F. M., J. H. Lawrence, E. V. Bridge, and O. L. Williams. Protective effects of preoxygenation with respect to abdominal gas pain resulting from decompression to 38,000 feet. CAM Report No. 353, 1 Sept. 1944.

128. Hetherington, A. W., and R. A. Miller. The effect of intravenous nitrogen on the respiration and circulation of the cat. Fed. Proc. 5:46 (1946).

129. Hill, L. Caisson disease. New York: Longmans, Green and Co., 1912.

130. Hill, L., and J. J. R. Macleod. The influence of compressed air and oxygen on the gases of the blood. J. Physiol. 29:382 (1903).

131. Hitchcock, M. A., and F. A. Hitchcock. Bert's barometric pressure. (Translation) Columbus, Ohio: College Book Company, 1943.

132. Hodes, R., and M. G. Larrabee. The relation between alveolar carbon dioxide tension and susceptibility to decompression sickness. Amer. J. Physiol. 147:603 (1946).

133. Hoff, E. C. A bibliographical sourcebook of compressed air: Diving and submarine medicine, p. 123. Washington: U.S. Government Printing Office, Feb. 1948.

134. Hoff, E. C., and J. F. Fulton. A bibliography of aviation medicine. Springfield, Ill.: Charles C Thomas, 1942 (supp. 1944).

135. Houston, C. S. Occurrence of bends, scotomata, and hemianopsia at altitudes below 20,000 feet. J. Aviation Med. 18:165 (1947).

136. Houston, C. S. A study of the physiological changes which occur during acclimatization to high altitude. Project X-720 (Av-376-s), Report No. 2, U.S. Navy School of Aviation Medicine, Pensacola, Fla., 4 Sept. 1946.

137. Houston, C. S., S. Nuzie, C. P. Seitz, and G. E. Besson. Studies on factors affecting incidence of bends in low pressure chamber runs. Research Project X-374, Report No. 2, Altitude Training Unit USNAS, Miami, Fla., 27 July 1944.

138. Hutchins, H. C., and O. E. Reynolds. Experimental investigation of the referred pain of aerodontalgia. J. Dent. Res. 26:3 (1947).

139. Hyman, C., and N. North. The effect of pressure breathing on the occurrence of decompression sickness. CAM Report No. 470, 19 Sept. 1945.

140. Ivy, A. C. Lectures in gastrointestinal physiology at Northwestern University. Unpublished data.

141. Ivy, A. C., A. J. Atkinson, H. F. Adler, and W. L. Burkhardt. Pertaining to the effect of dextroamphetamine and of preoxygenation plus dextroamphetamine on the incidence of bends and incapacitating bends and chokes at 40,000 feet, for one hour. CAM Report No. 113, 23 Dec. 1942.

142. Ivy, A. C., A. J. Atkinson, H. F. Adler, W. L. Burkhardt, and A. F. Thometz. Incidence of symptoms of "bends and chokes" at 47,500 feet for one hour without exercise with intermittent pressure breathing. CAM Report No. 370, 6 Oct. 1944.

143. Ivy, A. C., W. L. Burkhardt, H. F. Adler, and A. J. Atkinson. Unpublished data.

144. Ivy, A. C., and J. W. Wedral. A roentgen study of bubble formation in dogs. Program of Aeromedical Association, Twenty-first Annual Meeting, Chicago, 29 May 1950.

145. Jacobs, M. H., and D. R. Stewart. Observations on the blood of albino rats following rapid decompression. CAM Report No. 76, Oct. 1942.

146. Jones, C. M. Digestive tract pain: Diagnosis and treatment; Experimental observations. New York: Macmillan, 1938.

147. Jones, H. B. Preoxygenation and the rate of nitrogen elimination with regard to decompression sickness. CAM Report No. 491, Oct. 1945.

148. Jones, H. B., E. Myers, and W. E. Berg. Gas exchange, circulation, and diffusion. OEM cmr 196, 10 Apr. 1945.

149. Jones, H. L., and A. A. Schiller. Subjective responses to small reductions in barometric pressures in subjects with functional joint pathology. Fed. Proc. 6:138 (1947).

150. Jongbloed, J. The composition of the alveolar air in man at altitudes up to 14,000 meters; partly without oxygen supply: The mechanical effect of very low atmospheric pressure. Int. Air Congr. (V Congress, The Hague), 2:1418 (1930).

151. Joseph, T. V., C. F. Gell, R. M. Carr, and M. C. Shelesnyak. Toothache and the aviator. U.S. Navy Med. Bull. 41:643 (1943).

152. Kahlstrom, S. C., C. C. Burton, and D. B. Phemister. Aseptic necrosis of bone: Infarction of bones incaisson disease resulting in encapsulated and calcified areas in diaphyses and arthritis deformans. Surg. Gynec. Obstet. 68:129 (1939).

153. Kantor, J. L., and J. A. Marks. A study of intestinal flatulence. Ann. Intern. Med. 3:403 (1929).

154. Karpovich, P. V. Relation between bends and physical fitness. AAF School of Aviation Medicine Report 192-1, Oct. 1943.

155. Kaufman, S. S., L. F. Nims, and J. Nyboer. Peripheral circulation and decompression illness at 38,000 feet. CAM Report No. 318, 15 June 1944.

156. Keil, F. C. The effects of low barometric pressure on the field of vision. AAF School of Aviation Medicine Report 158-1, June 1943.

157. Kennon, R. H., and C. M. Osborn. Relation of aerodontalgia to aerosinusitis. Air. Surg. Bull. 2:434 (1945).

158. Knisely, M. H. Methods and testing of therapeutic agents in relation to bends. CAM Report No. 473, Sept. 1945.

159. Knisely, M. H. Observations and interpretations of changes in circulation induced by aero-embolism. Eng-M-49-696-1C, Wright Field, 14 Jan. 1943.

160. Knisely, M. H., S. Gray, H. M. Peck, R. L. Nichols, L. Warner, and I. A. Orcutt. The effect of elevation of a limb on the development and severity of bends pain. CAM Report No. 196, 1 Oct. 1943.

161 Knisely, M. H., S. Gray, H. M. Peck, R. L. Nichols, L. Warner, I. A. Orcutt, and N. Anderson. Preliminary tests of the effect of intravenous aminophyllin in preventing or alleviating bends and chokes. CAM Report No. 195, 1 Oct. 1943.

162. Larkin, J. C., and D. T. Watts. A new concept of the bends and a method of increasing one's resistance. CAM Report No. 291, 1 Jan. 1944.

163. Larrabee, M. G., J. C. Lilly, J. H. Comroe, Jr., and R. Hodes. Decompression sickness during exposure to 38,000 feet, accompanied by exercise: Evaluation of a classification procedure. CAM Report No. 137, 9 June 1943.

164. Las Vegas Army Air Field Gunnery School, Las Vegas, Nev.

165. Lazarow, A., P. R. Patek, E. Bartosh, and G. H. Scott. Observations on the capillary circulation in skeletal muscle of frogs at simulated high altitudes. CAM Report No. 162, 15 June 1943.

166. Lewis, T. Experiments relating to cutaneous hyperalgesia and its spread through somatic nerves. Clin. Sci. 2:373 (1936).

167. Lewis, T. Pain. New York: Macmillan, 1942.

168. Lund, D. W., and J. H. Lawrence. Studies on the cause of pain in high altitude "bends." Fed. Proc. 5(pt.2):66 (1946).

169. Mahady, S. C. F. A study of the blood and cardiovascular system following exposure to a simulated altitude of 38,000 feet. AAF School of Aviation Medicine Report 207-1, Nov. 1943.

170. Masland, R. L. Altitude tolerance when breathing oxygen and when breathing oxygen supplied under positive pressure. AAF School of Aviation Medicine Report 313-1, Aug. 1944.

171. Masland, R. L. Review of cases of collapse occurring in altitude chambers. AAF School of Aviation Medicine Report 172-1, Aug. 1943.

172. Matthews, B. H. C., and C. A. Carmichael. Chronological development of symptoms in "bends" in subjects breathing pure oxygen, with neurological report. CAM Report No. 22, 5 Oct. 1940.

173. McDill Field CCTS, Altitude Training Unit, Jan. 1943 to July 1946. (Unpublished data)

174. McDonough, F. E. Roentgenographic observation on the amount and distribution of intestinal gas at altitude in relation to abdominal symptoms. AAF School of Aviation Medicine Report 193-1, Nov. 1943.

175. McDowell, R. M. The loss of dental fillings by aviators engaged in high altitude flights. Dent. Bull. 6:195 (1935).

176. McElroy, W. D., A. H. Whiteley, K. W. Cooper, D. C. Pease, G. H. Warren, and E. N. Harvey. Bubble formation in animals: VI. Physiological factors: The role of circulation and respiration. J. Cell. Comp. Physiol. 24:273 (1944).

177. McElroy, W. D., A. H. Whiteley, G. H. Warren, and E. N. Harvey. Bubble formation in animals: IV. The relative importance of carbon dioxide concentration and mechanical tension during muscle contraction. J. Cell. Comp. Physiol. 24:133 (1944).

178. McIver, M. A., A. C. Redfield, and E. B. Benedict. Gaseous exchange between the blood and the lumen of the stomach and intestines. Amer. J. Physiol. 76:92 (1926).

179. McLester, J. S. Memorandum on intestinal gas. Subcommittee on Medical Nutrition, CAM Report No. 59, 14 July 1942.

180. Mitchell, D. F. Aerodontalgia. Bull. U.S. Army Med. Dept. No. 73:62 (1944).

181. Mitchell, D. F. A history of aviation dentistry. Annals of Dentistry 5: Nos. 1 and 2. June-Sept. 1946.

182. Moore, R. M., and C. W. Braselton, Jr. Injections of air and of carbon dioxide into a pulmonary vein. Ann. Surg. 112:212 (1948).

183. Motley, H. L., H. I. Chinn, and F. A. Odell. Studies on bends. J. Aviation Med. 16:210 (1945).

184. Observations on decompression sickness in man. RAF Physiological Research Unit, Farnborough FPRC 267, 27 Mar. 1941.

185. Pace, N. Equations for the estimation of total body fat and total body water from the solubility of inert gases in the body. Naval Med. Research Inst. Project X-191, Rep. No. 4, 25 Sept. 1945.

186. Patek, P. R., A. Lazarow, E. Bartosh, and G. H. Scott. Observation on living periosteum and periotoneum at simulated high altitudes. CAM Report 244, 17 Jan. 1944.

187. Physiology of flight. AAF Manual 25-60-2, pp. 41, 29 Aug. 1947.

188. Piccard, J. Aero-emphysema and the birth of gas bubbles. Proc. Mayo Clin. 16:700 (1941).

189. Pichotka, J. Experimental investigations concerning the cause of oxygen poisoning. (Translation from German) 28 Feb. 1946.

190. Pigott, J. P. Dental pain at high altitudes: Origin and treatment. CAM Report No. 383, 23 Oct. 1944.

191. Polland, W. S., and A. L. Bloomfield. Experimental referred pain from the gastrointestinal tract. J. Clin. Invest. 10:435-453 (1931).

192. Rangell, L. Cerebral air embolism. J. Nerv. Ment. Dis. 96:542 (1942).

193. Rathbun, E. N., and N. Pace. Studies on body composition: I. The determination of total body fat by means of the body specific gravity. Naval Med. Research Inst. Project X-191, Rep. No. 1, 7 Aug. 1944.

194. Reed, E., and L. R. Blinks. Bubble formation in decompressed animals: V. The relation of temperature and exercise to bubble formation in rats and tourniqueted legs of rabbits and goats. Report No. 379, NRC, 15 Oct. 1944.

195. Reed, E., and L. R. Blinks. Bubble formation in decompressed animals: VI. Vasoconstriction and the relation of the vascular bed to bubble formation in frogs. CAM Report No. 379, 15 Oct. 1944.

196. Rendich, R. A., and L. A. Harrington. Roentgen findings in caisson disease of bone with case reports. Radiology 35:439 (1940).

197. Revici, E., E. Stoopen, E. Frenk, and R. A. Ravich. The painful focus: II. The relation of pain to local physico-chemical changes. Bull. Inst. Appl. Biol. 1:21 (1949).

198. Reynolds, O. E., and H. C. Hutchins. Reduction of central hyperirritability following block anaesthesia of peripheral nerve, pp. 199. Symposium on Military Physiology. Digest Series No. 4 GE 61/1. 4-6 Dec. 1947.

199. Reynolds, O. E., H. C. Hutchins, A. Y. Werner, and F. R. Philbrook. Aerodontalgia occurring during oxygen indoctrination in the low pressure chamber. U.S. Nav. Med. Bull. 46:845 (1946).

200. Richardson, H. F., B. C. Coles, and G. E. Hall. Experimental gas embolism: I. Intravenous air embolism. Canad. Med. Ass. J. 36:584 (1937).

201. Ringsted, A., and K. Anderson. Experiments on oxygen therapy in experimental meteorism. Acta Chir. Scand. 90:529 (1944-1945).

202. Robinson, T. W., and D. P. Donnelly. High altitude tolerance tests. Aero-Medical Laboratory, ENG-49-696-1G, 12 May 1944.

203. Rodbard, S. Occurrence of decompression sickness on descent from high altitudes. J. Aviation Med. 17:89 (1946).

204. Romano, J., G. L. Engel, E. B. Ferris, Jr., H. W. Ryder, J. P. Webb, and M. A. Blankenhorn. Problems of fatigue as illustrated by experiences in the decompression chamber. War Med. 6:102 (1944,.

205. Romano, J., G. L. Engel, J. P. Webb, E. B. Ferris, H. W. Ryder, and M. A. Blankenhorn. Syncopal reactions during simulated high altitude exposures in the decompression chamber. CAM Report No. 128, 26 Apr. 1943.

206. Ruge, E. Beitraege zur Kentnis der Darmgase. Chem. Zentralbl. 7:347 (1862).

207. Ryder, H. W., G. L. Engel, J. Romano, J. P. Webb, M. A. Blankenhorn, E. B. Ferris, and W. E. Brown. An assay of dextroamphetamine for its protective value in decompression sickness. CAM Report No. 112, 28 Jan. 1943.

208. Salt Lake City Altitude Training Unit, 1943. (Unpublished data)

209. Sandler, H. C. Toothache at low atmospheric pressures. Milit. Surg. 97:475 (1945).

210. Santa Ana (Calif.) 33d Altitude Training Unit, 1943. (Unpublished data)

211. Savely, H. E. High altitude classification tests. CAM Report No. 99, 31 Oct. 1942.

212. Shilling, C. W. Compressed air illness. U.S. Nav. Med. Bull. 39:367 (1941).

213. Shilling, C. W., J. A. Hawkins, I. B. Polak, and R. A. Hansen. Caisson disease and its relation to tissue saturation with nitrogen. U.S. Nav. Med. Bull. 33:434 (1935).

214. Smaller, B., and M. M. Kennedy. Preselection test for susceptibility to aero-embolism. Aero-Medical Laboratory Project ENG-M-49-695-27, 30 Mar. 1943.

215. Smedal, H. A. Change in resistance to decompression. CAM Report No. 92, 20 Nov. 1942.

216. Smedal, H. A., E. B. Brown, and C. E. Hoffman. Incidence of bends pain in a short exposure to simulated altitudes of 26,000, 28,000, and 30,000 feet. J. Aviation Med. 17:67 (1946).

217. Smedal, H. A., and A. Graybiel. Effects of decompression on thirty-five subjects repeatedly exposed to a simulated altitude of 20,000 feet during approximately one month. Project X-762 (AV-39-k), Report No. 1, U.S. Navy School of Aviation Medicine, Pensacola, Fla., 1 Sept. 1947.

218. Smith, H. W. The effect of anoxia on the incidence of decompression sickness at 35,000 feet. Number 2 Clinical Investigation Unit, RCAF, Regina. Report to Director of Medical Sciences (Air), Jan. 1943.

219. Smith, H. W., and G. W. Manning. The relationship between daily urinary output and the incidence of decompression sickness. Number 2 Clinical Investigation Unit, RCAF, Aug. 1942.

220. Smith, H. W., C. B. Stewart, and H. A. McAlpine. The effect of mild exercise on the incidence of decompression sickness on consecutive daily ascents to 35,000 feet. Number 2 Clinical Investigation Unit, RCAF, Regina. Report to Director of Medical Services (Air), May 1942.

221. Smith, P. K. Effects of morphine at high altitude. AAF School of Aviation Medicine Report 181-1, Sept. 1943.

222. Smith, P. K. The use of morphine at high altitudes for the relief of decompression pain. AAF School of Aviation Medicine Report 175-1, Sept. 1943.

223. Stevens, C. D., M. Inatome, H. W. Ryder, E. B. Ferris, M. A. Blankenhorn, B. V. Ratterman, and J. K. Friedlander. The rate of nitrogen elimination from the lungs and its relation to individual susceptibility to decompression sickness. CAM Report No. 456, July 1945.

224. Stevens, C. D., H. W. Ryder, E. B. Ferris, Jr., G. L. Engel, J. P. Webb, F. Senior, and J. K. Friedlander. The rate of nitrogen elimination from the lungs; its relation to susceptibility to decompression sickness. CAM Report No. 237, Dec. 1943.

225. Stewart, C. B., and G. K. MacIntosh. A study of dental conditions associated with discomfort at high altitude. Number One "Y" Depot, RCAF, Halifax. NRC, Apr. 1943.

226. Stewart, C. B., and H. W. Smith. A comparison of the incidence of decompression sickness at 35,000 and 40,000 feet. Number 1 Clinical Investigation Unit, Report No. B167, RCAF, Toronto, 30 Apr. 1945.

227. Stewart, C. B., and H. W. Smith. The effect of reascent on the recurrence of decompression sickness. Number One "Y" Depot, RCAF, Oct. 1943.

228. Stewart, C. B., H. W. Smith, H. A. McAlpine, O. H. Warwick, and G. W. Manning. The incidence of decompression sickness on consecutive daily ascents to 35,000 feet. Number 2 Clinical Investigation Unit, RCAF, Regina. Associate Committee on Aviation Medical Research, NRC, July 1942.

229. Stewart, C. B., O. H. Warwick, J. W. Thompson, G. L. Bateman, D. J. Milne, and D. E. Gray. Relation of certain factors to the incidence of decompression sickness. Flying Personnel Medical Section. Number One "Y" Depot, RCAF, Halifax, Mar. 1943.

230. Stewart, C. B., O. H. Warwick, J. W. Thompson, G. L. Bateman, D. J. Milne, and D. E. Gray. A study of decompression sickness. Flying Personnel Medical Section. Number One "Y" Depot, RCAF, Halifax, Mar. 1943.

231. Swann, E. G., and T. B. Rosenthal. A survey of the incidence of decompression sickness with reference to some constitutional and environmental variants. 31st Altitude Training Unit Report, 10 Mar. 1944.

232. Sweeney, H. M. Explosive decompression: Human subjects. Aero-Medical Laboratory, ENG. 49-695-29F, 10 Aug. 1944.

233. Swindle, P. F. The possible relationship between intravascular agglutination of erythrocytes and decompression sickness. CAM Report No. 178, 13 Aug. 1943.

234. Taylor, C. B., and F. J. Robinson. Flatulence at altitude in the presence of cardiospasm. J. Aviation Med. 16:272 (1945).

235. Taylor, H. K. Aseptic necrosis in bone infarcts in caisson and non-caisson workers. New York J. Med. 43:2390 (1943).

236. Templeton, F. Quoted by Palmer, W. F. The pain of peptic ulcer. *In* Wolff, H. G., H. S. Gasser, and J. C. Hinsey (eds.) Pain, p. 308. Baltimore: Williams & Wilkins, 1943.

237. Teschendorf, W. Ueber die Resorptionzoit von Gason in der Brusthoele. Arch. Exp. Path. u. Pharmakol. 104:352 (1924).

238. Thomas, S. F., and O. L. Williams. High altitude joint pains (bends): Their roentgenographic aspects. Radiology 44:259 (1945).

239. Thompson, J. W., J. Sharpe, and J. R. Brett. The incidence of decompression sickness in aircrew and its prevention. Appendix P, Proceedings of 15th Meeting of ACAMR (NRC), 26 June 1942.

240. Thompson, J. W., C. B. Stewart, O. H. Warwick, G. L. Bateman, D. J. Milne, and D. E. Gray. Relationship of certain factors to the incidence of decompression sickness. Appendix II, Report to NRC, Canada, FPMS No. D-3, Apr. 1944.

241. Tillisch, J. H. The effect of diet on gastrointestinal symptoms at altitude. AAF School of Aviation Medicine Report 208-1, Aug. 1944.

242. Tobias, C. A., J. H. Lawrence, H. B. Jones, and W. R. Lyons. Circulation and decompression sickness. II. CAM Report No. 352, 29 Aug. 1944.

243. Tobias, C. A., W. F. Loomis, F. C. Henry, W. R. Lyons, H. B. Jones, W. N. Sears, S. F. Cook, J. B. Mohney, J. G. Hamilton, and J. H. Lawrence. Circulation and decompression sickness. CAM Report No. 144, 7 June 1943.

244. Tobias, C. A., W. F. Loomis, and J. H. Lawrence. Studies on skin temperature and circulation in decompression sickness. Amer. J. Physiol. 149:626 (1947).

245. Tobias, C. A., W. R. Lyons, O. L. Williams, E. V. Bridge, J. H. Lawrence, H. F. Helmholz, Jr., and A. R. Sweeney, Jr. A study of decompression sickness in 25 airplane flights at 35,000 feet. CAM Report No. 319, May 1944.

246. Twynam, G. E. A case of caisson disease. Brit. Med. J. 1:190 (1888).

247. Van Allen, C. M., L. S. Hrdina, and J. Clark. Air embolism from pulmonary vein; clinical and experimental study. Arch. Surg. (Chicago) 19:567 (1929).

248. Wanger, C. E. Observations of gas bubbles in pial vessels of cats following rapid decompression from high pressure atmospheres. J. Neurophysiol. 8:29 (1945).

249. Warwick, O. H. The apparent relationship of fluid balance to the incidence of decompression sickness. Number 2 Clinical Investigation Unit, RCAF, Regina. Report to NRC, Apr. 1942.

250. Warwick, O. H. Further studies on the relationship of fluid intake and output to the incidence of decompression sickness. Flying Personnel Medical Section. Number One "Y" Depot, RCAF, Halifax. Report to NRC, Feb. 1943.

251. Webb, J. P., G. L. Engel, C. D. Stevens, and E. B. Ferris, Jr. The effect of pressure breathing on decompression sickness under different altitude conditions. CAM Report No. 385, 30 Oct. 1944.

252. Webb, J. P., E. B. Ferris, G. L. Engel, J. Romano, H. W. Ryder, C. D. Stevens, and M. A. Blankenhorn. Radiographic studies of the knee during bends. CAM Report No. 30c, 8 May 1944.

253. Webb, J. P., H. W. Ryder, G. L. Engel, J. Romano, M. A. Blankenhorn, and E. B. Ferris. The effect on susceptibility to decompression sickness of preflight oxygen inhalation at rest as compared to oxygen inhalation during strenuous exercise. CAM Report No. 134, 5 May 1943.

254. Whitaker, D. M., L. R. Blinks, W. E. Berg, V. C. Twitty, and M. Harris. Muscular activity and bubble formation in animals decompressed to simulated altitudes. J. Gen. Physiol. 28:215 (1945).

255. Whitaker, D. M., L. R. Blinks, V. C. Twitty, R. B. Dean, W. E. Berg, and M. Harris. Further experiments on bubble formation. CAM Report No. 84, 19 Nov. 1942.

256. Whitehorn, W. V., A. Lein, and A. Edelmann. The general tolerance and cardiovascular responses of animals to explosive decompression. Amer. J. Physiol. 147:289 (1946).

257. Whiteley, A. H., W. D. McElroy, G. H. Warren, and E. N. Harvey. Bubble formation in animals: V. Denitrogenation. J. Cell. Comp. Physiol. 24:257 (1944).

258. Wigodsky, H. S. Repeated low pressure chamber flights as an improved procedure for high altitude classification. AAF School of Aviation Medicine Report 67-1, July 1942.

259. Woodyatt, R. T., and E. A. Graham. Alimentary respiration. The secretion of $CO_2$ by alimentary mucosa and its relation to eructations of gas and abnormal inflation of the stomach and intestine. Ohio Med. J. 8:407 (1912).